SUMMARY OF SAFETY & EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Prosthesis, Intervertebral Disc
Device Trade Name:	pro**disc**® L Total Disc Replacement
Device Product Code:	MJO
Applicant's Name and Address:	Centinel Spine, LLC 900 Airport Rd, 3B West Chester, PA 19380 USA
Date(s) of Panel Recommendation:	N/A
Premarket Approval Application: (PMA Number)	P050010/S020
Date of FDA Notice of Approval:	April 10, 2020

The original PMA (P050010) was approved on August 14, 2006 and is indicated for spinal arthroplasty in skeletally mature patients with degenerative disc disease (DDD) at one level from L3-S1. DDD is defined as discogenic back pain with degeneration of the disc confirmed by patient history and radiographic studies. These DDD patients should have no more than Grade 1 spondylolisthesis at the involved level. Patients receiving the pro**disc**® L Total Disc Replacement should have failed at least six months of conservative treatment prior to implantation of the pro**disc**® L Total Disc Replacement. The SSED to support the previously approved one level indication is available on the CDRH website (https://www.accessdata.fda.gov/cdrh_docs/pdf5/P050010B.pdf) and is incorporated by reference here. The current supplement was submitted to expand the indication for the pro**disc**® L to include use of the device at two (2) contiguous intervertebral level(s).

II. INDICATIONS FOR USE

The pro**disc**® L ("pro**disc**® L") Total Disc Replacement is indicated for spinal arthroplasty in skeletally mature patients with degenerative disc disease (DDD) at one or two contiguous intervertebral level(s) from L3-S1. DDD is defined as discogenic back pain with degeneration of the disc confirmed by patient history and radiographic studies. These DDD patients should have no more than Grade 1 spondylolisthesis at the involved level(s). Patients receiving the pro**disc**® L Total Disc Replacement should have failed at least six months of conservative treatment prior to implantation of the pro**disc**® L Total Disc Replacement.

III. CONTRAINDICATIONS

The pro**disc**® L Total Disc Replacement should not be implanted in patients with the following conditions:

- Active systemic infection or infection localized to the site of implantation
- Osteopenia or osteoporosis defined as DEXA bone density measured T-score < -1.0
- Bony lumbar spinal stenosis
- Allergy or sensitivity to implant materials (cobalt, chromium, molybdenum, polyethylene, titanium)
- Isolated radicular compression syndromes, especially due to disc herniation
- Pars defect
- Involved vertebral endplate that is dimensionally smaller than 34.5mm in the medial-lateral and/or 27mm in the anterior-posterior directions
- Clinically compromised vertebral bodies at the affected level due to current or past trauma
- Lytic spondylolisthesis or degenerative spondylolisthesis of grade > 1

IV. WARNINGS AND PRECAUTIONS

Please refer to the pro**disc**® L Instructions for Use for warnings and precautions.

V. DEVICE DESCRIPTION

The pro**disc**® L two-level device that is the subject of this PMA supplement is identical to the currently marketed pro**disc**® L one-level device (P050010). The pro**disc**® L is a weight-bearing modular implant consisting of two endplates and one polyethylene inlay. The pro**disc**® L endplates are manufactured from cobalt-chromium alloy and are available in two sizes (medium and large).

The superior endplates are available in three lordotic angles (3°, 6°, 11°) and the inferior endplates are also available in three lordotic angles (0°, 3°, 8°). The surfaces of both inferior and superior endplates are plasma sprayed with commercially pure (CP) titanium. Fixation of the pro**disc**® L to the vertebral bodies is intended through bony ingrowth, with initial stabilization by a large central keel and two small spikes on the surface of the two endplates. The inlays are manufactured from ultra-high molecular weight polyethylene (UHMWPE), and are available in three heights (10, 12, and 14mm) with anterior-posterior and lateral sizing consistent with the endplate sizing. The Range of Motion (ROM) allowed by the pro**disc**® L is 13° of flexion, 7° of extension, ±10° of lateral bending, and ±3° of axial rotation, as measured through in vitro testing. The maximum ROM allowed by an assembled pro**disc**® L device is dependent on the endplate size and inlay height selected. The ROM experienced in flexion, extension, and lateral bending *in vivo* may be less than the maximum ROM of the implant itself due to anatomical constraints. As the pro**disc**® L device is constrained with respect to rotational motion, ROM experienced in rotation is entirely dependent on anatomical constraints.

Figure 1: prodisc® L device

The superior and inferior endplates of pro**disc**® L are manufactured of Co-28Cr-6Mo (CoCrMo) per ISO 5832-12. The surfaces of both the inferior and superior endplates are plasma sprayed with commercially pure titanium (CpTi) conforming to ISO/DIS 5832-2 (1999) "Implants for surgery". The fixation of the implant to the vertebral bodies is intended to be achieved through bone ongrowth, with initial stabilization by a keel and two small spikes on the surface of the two endplates. The inlays are manufactured from UHMWPE. For identification of the position of the UHMWPE-inlay under x-ray-control, they include a tantalum x-ray marker per ISO 13782. The inlay snap-locks into the inferior plate and provides the inferior convex bearing surface that articulates with the concave bearing surface of the superior plate.

Table 1 and Table 2 describe the available sizes and configurations of the pro**disc**® L Total Disc Replacement components:

Table 1: prodisc® L Endplates

Size	Approximate Dimensions		Angles (degrees)
	Anterior/Posterior width (mm)	Lateral width (mm)	
Inferior Endplate – Medium	27	34.5	0 °
Inferior Endplate – Medium	27	34.5	3°
Inferior Endplate – Medium	27	34.5	8°
Inferior Endplate – Large	30	39	0 °
Inferior Endplate – Large	30	39	3°
Inferior Endplate – Large	30	39	8°
Superior Endplate – Medium	27	34.5	3°
Superior Endplate – Medium	27	34.5	6 °
Superior Endplate – Medium	27	34.5	11 °
Superior Endplate – Large	30	39	3°
Superior Endplate – Large	30	39	6 °
Superior Endplate – Large	30	39	11 °

Table 2: prodisc® L Inlays

Size	Approximate Dimensions		Height (mm) (Assembled)
	Anterior/Posterior width (mm)	Lateral width (mm)	
PE Inlay – Medium	26	23	10
PE Inlay – Medium	26	23	12
PE Inlay – Medium	26	23	14
PE Inlay – Large	29	25	10
PE Inlay – Large	29	25	12
PE Inlay – Large	29	25	14

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of DDD at two contiguous intervertebral level(s) from L3-S1.

- Nonoperative alternative treatments include, but are not limited to, activity restriction, physical therapy, back exercises, chiropractic care, medication and spinal injections.
- Surgical alternatives include, but are not limited to, surgical decompression and/or fusion using various bone grafting techniques or interbody fusion devices, which may or may not be used in conjunction with anterior/anterolateral spinal systems (e.g., plate and screw systems), or posterior spinal systems (e.g., pedicle screw/rod or hook/wire/rod systems).

Each alternative has advantages and disadvantages. Patients should fully discuss the available alternatives with his or her physician to select the option that best meets their clinical condition, lifestyle and expectations.

VII. MARKETING HISTORY

The pro**disc**® L Total Disc Replacement has been commercially available in markets outside of the United States since 1990 and is currently available without restrictions on the number of levels implanted. The pro**disc**® L was approved by the FDA on August 14, 2006 (P050010) for single level implantation. More than 17,900 pro**disc**® L devices have been sold within the US as of September 2018 (Table 3).

Table 3: prodisc® L Marketing History

Markets	**Units Sold (2004 – 2018)**
US*	17,983
Outside the US (oUS)	30,601
Global TOTAL	**48,584**

* Commercial Distribution within the United States after PMA approval in 2006.

The pro**disc**® L Total Disc Replacement has not been withdrawn from marketing for any reason related to its safety or effectiveness. The pro**disc**® L Total Disc Replacement is commercially available in the following countries outside of the United States:

Argentina Croatia Iran New Zealand South Africa

Australia	Czech Republic	Ireland	Norway	South Korea
Austria	Denmark	India	Panama	Spain
Belgium	Ecuador	Israel	Peru	Sweden
Brazil	Egypt	Italy	Poland	Switzerland
Bulgaria	Finland	Jamaica	Portugal	Taiwan
Canada	France	Libya	Romania	Thailand
Chile	Germany	Luxembourg	Russia	Turkey
China	Greece	Malaysia	Saudi Arabia	United Arab Emirates
Columbia	Hong Kong	Mexico	Singapore	United Kingdom
Costa Rica	Hungary	Netherlands	Slovakia	Venezuela

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device. These adverse effects include: 1) those commonly associated with any surgical procedure; 2) those specifically associated with lumbar spinal surgery using an anterior approach; and, 3) those associated with a total disc replacement device (including the pro**disc**® L Total Disc Replacement).

General Surgery Adverse Effects

General surgical adverse effects include, but are not limited to:

- Anesthetic reaction
- Hematoma
- Ileus requiring nasogastric tube
- Infection (wound, local and/or systemic)
- Abscess
- Wound dehiscence
- Wound necrosis
- Edema
- Heart and vascular complications
- Hypotension
- Ischemia
- Hemorrhage
- Thrombosis including deep vein thrombosis
- Embolism including pulmonary embolism
- Pulmonary complications
- Gastrointestinal and/or genitourinary complications
- Seizures
- Nerve damage
- Vascular damage resulting in catastrophic or fatal bleeding
- Paralysis,
- Reflex sympathetic dystrophy
- Changes to mental status
- Complications of pregnancy including miscarriage and congenital defects
- Inability to resume activities of daily living
- Death

Anterior Lumbar Surgery Adverse Effects

Anterior lumbar surgical adverse effects include, but are not limited to:

- Bowel injury or perforation
- Epidural hematoma
- Hernia
- Peritoneal adhesions
- Retroperitoneal hematoma
- Injury to kidneys or ureters
- Nerve damage due to surgical trauma

- Neurological complications, including bowel and/or bladder dysfunction, impotence, tethering of nerves in scar tissue, muscle weakness or paresthesias
- Damage to lymphatic vessels and/or lymphatic fluid exudation
- Fracture of vertebral bony structures
- Peritonitis
- Scarring
- Injury to neural structures possibly resulting in neurologic deficits including paralysis or chronic pain
- Dural tears or leaks
- Surrounding soft tissue damage

Lumbar Total Disc Replacement Adverse Effects

Adverse effects specific to lumbar artificial discs, including the pro**disc**® L, are but may not be limited to:

- Expulsion or retropulsion, causing pain, paralysis, vascular or neurological damage
- Impingement or damage to neural structures
- Need for additional surgery including removal of the pro**disc**® L
- Failure of the device/procedure to improve symptoms and/or function
- Wear debris (polyethylene or metal) generation leading to an adverse local tissue reaction that may cause implant loosening or failure
- Early or late loosening of the device components
- Implant malpositioning which can lead to erosion into adjacent large arteries and veins and cause catastrophic bleeding in the late post-operative period
- Implant breakage, disassembly, bending, dislodgement, or migration
- Spondylolysis
- Spondylolisthesis
- Spinal stenosis
- Change in lumbar lordosis
- Instability of the spine
- Facet joint degeneration
- Foreign body reaction to the implant including possible tumor formation, autoimmune disease, metallosis, and/or scarring
- Bone resorption
- Calcification resulting in bridging trabecular bone (heterotopic ossification) and fusion either at the treated level or adjacent levels
- Annular ossification
- Bending or breakage of pro**disc**® L instruments including the possibility that fragments may remain in the patient
- Sizing issues with device components
- Anatomical or technical difficulties placing the device
- Loss of disc height
- Herniation or degeneration of adjacent discs
- Tissue or nerve damage caused by improper positioning or placement of the device or instruments

For the specific adverse events that occurred in the pro**disc**® L clinical study, please see Section X below.

IX. SUMMARY OF NONCLINICAL STUDIES

A summary of previously reported nonclinical studies can be found in the SSED for the original PMA and are incorporated by reference here

(https://www.accessdata.fda.gov/cdrh_docs/pdf5/P050010B.pdf). Additional testing performed to support the two-level indication are provided below (
Table 4).

- Wear Mode I (General ROM)
- Wear Mode IV (Impingement)
- Static Axial Compression
- Dynamic Axial Compression
- Static Compression Shear
- Dynamic Compression Shear
- Subluxation
- Subsidence
- Static Inlay Expulsion
- Expulsion
- Magnetic Resonance Safety
- Retrieval Analysis

Table 4: Nonclinical Testing

Test Description	Purpose	Acceptance Criteria	Results
Wear Mode I (General ROM)	Evaluate the Mode I wear performance of the pro**disc**® L total disc replacement.	Specifically, a six-degree-of-freedom spine wear simulator (MTS, Eden Prairie, MN) was used for testing on the smallest and largest pro**disc**® L constructs. The polyethylene inserts were imaged using a µCT 80 (Scanco Medical AG, Switzerland) at a maximum voxel resolution of 18 µm. The device components were scanned at 0.0 million cycles (MC) and 5.0 MC. A custom Matlab code was written in order to calculate the dimensional changes on each device. ISO 18192-1:2011, ASTM F2423-11 Acceptance Criteria: Less than 30mg/million cycles	The average mass wear rate of the polyethylene insert through 5.0 MC was 5.4 ± 1.3 mg/MC and 4.8 ± 1.1 mg/MC for the large and medium size devices, respectively.

Test Description	Purpose	Acceptance Criteria	Results
Wear Mode IV (Impingement)	The objective of this study was to evaluate the Mode IV wear (impingement) performance of the Centinel Spine pro**disc**® L total disc replacement.	Through the modeling and sub sequential experimental validation, it was concluded that the large, 11° lordotic angle superior device would be tested using an initial impingement angle of 12°. Overall, the impingement conditions included ± 2° axial rotation, 1200 N static compressive axial load, and 12 ± 2 flexion/extension for both the aligned and 2mm anterior offset test groups. ASTM F3295-18, ISO 14243-2:2009, ISO 18192-1:2011, ISO 181912-3:2017, ASTM F2423-11 Acceptance Criteria: 1. Wear mechanism at the impingement location for the no offset condition will be similar based on the observed wear and damage patterns. 2. The average wear rates demonstrated by this impingement testing for the no offset condition should be found to be less than or equal to the Mode I average wear rates at 1 Mc. The no offset condition should only induce wear in the polyethylene component. If the wear mechanism was found to be similar the wear rate for the UHMWPE is also expected to be comparable.	Under impingement conditions, the rate of mass loss of the polyethylene insert was less than in the Mode I testing condition. The polyethylene demonstrated impingement on the posterior surface. Characteristic of the contact observed on published retrievals, metal-on-metal contact was observed in the 2 mm offset test group. The maximum mass loss experienced by the metal components was converted to maximum volume losses of 0.6 mm^3 and 0.5 mm^3 for the inferior and superior components, respectively.
Static Axial Compression	The objective of this test was to characterize the performance of the pro**disc**® L outside of the US (oUS) Centinel Spine manufactured parts under static axial compression loading	The static axial compression tests were performed in displacement control at a rate of 12 mm/minute. Force and displacement data were recorded using the test system controller software. The ramp waveform was performed until the load cell limit or until gross failure occurred. ASTM F2346-11 Acceptance Criteria: Greater than 1650N	The ultimate load for static compression testing was 24,517.3N±6.2N for the M10 pro**disc**® L oUS implant constructs, and 24,518.1N±8.5N for the L14 pro**disc**® L oUS implant constructs.
Dynamic Axial Compression	The objective of this test was to characterize the performance of the pro**disc**® L oUS Centinel Spine manufactured parts under dynamic axial compression loading.	A cyclic force with a constant frequency of 5 Hz was applied to each specimen. The forces were maintained with a constant sinusoidal force amplitude control at a constant force ratio (R=min/max) equal to 10. Testing was terminated when the specimen reached the endurance value of 10,000,000 cycles or failure defined as displacement in excess of 1 mm before 500 cycles resulting in permanent deformation of the inlay and/or displacement in excess of 1 mm from the displacement at 500 cycles resulting in permanent deformation of the inlay. ASTM F2346-11 Acceptance Criteria: Greater than 1650N	The axial compression runout loads for both, the M10 and the L14 pro**disc**® L oUS implant constructs was 4000N, which is greater than the acceptance criteria of 1650N.

Test Description	Purpose	Acceptance Criteria	Results
Static Compression Shear	The objective of this test was to characterize the performance of the pro**disc**® L oUS Centinel Spine manufactured parts under static compression shear loading.	The specimen was placed within the pockets of the test blocks. These test blocks were placed within the pockets of the custom adapter plates and attached to the rigid superior and inferior 45º fixtures, which were in-line with the actuator. The static shear tests were performed in displacement control at a rate of 12 mm/minute. Force and displacement data were recorded using the test system controller software. The ramp waveform was performed until the load cell limit or until gross failure occurred. ASTM F2346-11 Acceptance Criteria: Greater than 1650N	The ultimate load for static compression-shear testing was 6,758.7N±128.8N for the M10 pro**disc**® L oUS implant constructs, and 10,467.9±1422.1N for the L14 pro**disc**® L oUS implant constructs.
Dynamic Compression Shear	The objective of this test was to characterize the performance of the pro**disc**® L oUS Centinel Spine manufactured parts under dynamic compression shear loading.	The specimen was placed within the pockets of the test blocks. These test blocks were placed within the pockets of the custom adapter plates and attached to the rigid superior and inferior 45º fixtures, which were in-line with the actuator. A cyclic force with a constant frequency of 5 Hz was applied to each specimen. The forces were maintained with a constant sinusoidal force amplitude control at a constant force ratio (R=min/max) equal to 10. Testing was terminated when the specimen reached the endurance value of 10,000,000 cycles or failure defined as displacement in excess of 2 mm from the displacement at 500 cycles resulting in permanent deformation of the inlay. A 2 mm displacement limit was set after 500 cycles to trigger a test stop and a specimen inspection. Macroscopic checks were performed approximately every 2,000,000 cycles. The failure mode of each specimen and the corresponding cycle count were recorded. Graphical representation of the fatigue data was also generated. ASTM F2346-11 Acceptance Criteria: Greater than 1650N	The dynamic compression-shear runout loads for M10 pro**disc**® L oUS implant constructs was 1650N, and 3250N for L14 pro**disc**® L oUS implant constructs.
Subluxation	The objective of this test was to characterize the pro**disc**® L oUS device resistance to subluxation.	M10 (N=3), and, L14 (N=3) pro**disc**® L oUS implant constructs were tested. The expulsion jig setup was positioned such that the loading axis was parallel to the device X-axis and the device positioned such that the X-axis loading was directed in the posterior to anterior direction. Testing was performed at a rate of 6 mm per minute until a significant reduction in force (>20% of measured force), fixture impingement, or until complete subluxation had occurred. Acceptance Criteria: Greater than 230N	The results show that the subluxation force was 275.1±2.5N for the M10 devices and 268.2±4.8N for the L14 devices.

Test Description	Purpose	Acceptance Criteria	Results
Subsidence	The objective of this test was to characterize the pro**disc**® L oUS implant construct's mechanical strength and durability.	Six (6) pro**disc**® L oUS implants were inserted into a foam block at a displacement rate control rate of 6mm/minute. Force and displacement data were recorded using the test system controller software. Maximum force was recorded. ASTM F2267-04(2018) Acceptance Criteria: Greater than 3400N	The results show that the subsidence force was 5103N for the M10 implant constructs.
Static Inlay Expulsion	The objective of this test was to characterize the force required to expulse the PE inlay from the inferior plate.	The inferior plate was machined down such that the point loaded could contact the inlay on the flat, posterior end. A 13.0 mm wide fixture was used to push against the M10 PDL oUS device during the test such that the load was only applied to the inlay. Testing was performed at a rate of 6 mm per minute until a significant reduction in force (>20% of measured force), fixture impingement, or at least 3 mm of displacement. Force and displacement data were recorded at a reasonable rate and saved for analysis to determine the displacement at expulsion strength (mm) and expulsion strength (N). Acceptance Criteria: Greater than 450N	The inlay expulsion force was 961±42N with a displacement of 2.45±0.63mm for the M10 Inlays and Inferior Plates. The inlay expulsion force and was 1,465±49N with a displacement of 1.59±0.10mm for the L14 Inlays and Inferior Plates.
Expulsion	The objective of this test was to characterize the expulsion force of an assembled implant construct from between simulated vertebral bodies.	The specimen/test block assembly were positioned in the expulsion fixture such that the foam test blocks are rigidly fixed, and a 450 N axial compressive force was applied to the device along the Z-axis. Testing was performed at a rate of 6 mm per minute until a significant reduction in force (>20% of measured force), fixture impingement, or at least 3 mm of displacement. Force and displacement data were recorded at a reasonable rate and saved for analysis to determine the displacement at expulsion strength (mm) and expulsion strength (N). Acceptance Criteria: Greater than 450N	The results show that the expulsion force was 1,125±31N with a displacement of 2.51±0.23mm for the M10 implant constructs. The expulsion force was 1,057±24N with a displacement of 2.43±0.58mm for the L14 implant constructs.

Test Description	Purpose	Acceptance Criteria	Results
Magnetic Resonance (MR) Safety	The objective of this test was to determine the conditions under which the implant could safely be in an MR environment.	The specimen was tested for magnetically induced displacement force by suspending the specimen from a thin string and placed at a specific location along the Z-axis of a 3.0 T MR scanner. The deflection angle was then calculated. ASMT F2052 The magnetically induced torque was evaluated qualitatively by manually turning the subject device at the isocenter of the 3.0 T magnet. ASTM F2213 The image artifact was measured using FFE and SE sequences in 1.5T and 3.0T MR scanners. ASTM F2119 The implant was placed in a phantom (gel-filled box). Temperature probes were placed on the implant at the locations of highest expected heating. The maximum temperature rise for a 15 minute scan of 2 W/kg was measured. ASTM F2182	The testing resulted in identifying the following conditions for use in an MR environment. Static Magnetic Field: 1.5 and 3.0 T. Maximum Spatial Gradient: 900 gauss/cm. Maximum MR-system reported SAR of 4 W/kg for 15 minutes.
Retrieval Analysis	The objective of this test was to evaluate the degradation processes evident in explanted implants.	Three retrieved devices (05103103, 05121601, and 06081002) underwent a Stage II analysis per ASTM F561, which included white light interferometry (WLI). Two of the three retrieved devices (05121601 and 06081002) underwent Micro-CT analysis to look for the presence of subsurface cracking which could be indicative of subsurface oxidation, as well as to calculate dimensional changes due to wear volume loss. Stage III analysis was not conducted and the retrieved devices showed no signs of oxidation (i.e. white-banding, cracking or discoloration), and did not need to be measured. ASTM F561 and ISO 12891-1	The measured surface roughness of the superior endplate was shown to increase. These findings are consistent with the observed adhesive abrasive damage mode which is common for orthopedic and spine UHMWPE-CoCr bearing surfaces. The roughness values were within the expected range for the observed damage and wear. There was no evidence of subsurface cracking that would be indicative of oxidation and no evidence of gross wear. Micro-CT wear maps were produced, and wear penetration was calculated, which ranged from 0.2 to 0.4 mm in penetration height loss. The penetration values were within the expected range for the observed damage and wear.

X. SUMMARY OF CLINICAL STUDIES

The applicant performed a clinical study to determine a reasonable assurance of safety and effectiveness of the pro**disc**® L for patients with contiguous two-level DDD between L3 and S1 who had not previously received fusion surgery at any intervertebral level, and who had failed to improve with conservative treatment for at least 6 months prior to enrollment. Data from this clinical study were the basis of the PMA Supplement approval decision. A summary of the clinical study is presented below.

A. Study Design

Under IDE G010133 (approved in 2001), a multi-center, prospective, randomized, controlled clinical trial in the US was conducted to evaluate the safety and effectiveness of pro**disc**® L total disc replacement. The control group was treated with circumferential fusion consisting of commercially available femoral ring allograft and posterolateral fusion with autogenous iliac crest bone graft in combination with a pedicle screw-rod system. The IDE study included both one-level and two-level arms. The following pertains to the clinical study results for subjects who were enrolled in the two-level arm of the study.

Subjects were treated between January 2002 and June 2004. The database for this PMA Supplement included 255 enrolled subjects who were randomized to either pro**disc**® L or Fusion. There were 19 investigational sites, of which 16 sites enrolled subjects in the two-level arm.

The two-level study was a multicenter, prospective, randomized clinical trial consisting of subjects with contiguous two-level DDD between L3 and S1 who had not previously received fusion surgery at any intervertebral level, and who had failed to improve with conservative treatment for at least 6 months prior to enrollment. Subjects were randomized to receive either the pro**disc**® L Total Disc Replacement or circumferential fusion according to a 2:1 ratio. The study followed subjects through 60 months follow up, with the primary endpoint assessed with data at 24 months.

Inclusion and exclusion criteria were identical to the one level IDE, with the exception of treatment at two levels rather than one level.

1. Clinical Inclusion and Exclusion Criteria

To be eligible for the study, subjects were required to meet all inclusion criteria and none of the exclusion criteria, which are presented below in Table 5.

Table 5: Study Inclusion/Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
• Degenerative Disc Disease (DDD) in two adjacent vertebral levels between L3 and S1. Diagnosis of DDD required, back and/or leg (radicular) pain; and radiographic confirmation of any of the following by CT, MRI, discography, plain film, myelography and/or flexion /extension films: o Instability (≥ 3mm translation or ≥ 5° angulation); o Decreased disc height > 2mm; o Scarring/thickening of annulus fibrosis; o Herniated nucleus pulposus; or o Vacuum phenomenon. • Age between 18 and 60 years. • Failed at least six months of conservative treatment. • Oswestry Low Back Pain Disability Questionnaire (Oswestry Disability Index, ODI) score of at least 20/50 (40%) (Interpreted as moderate/severe disability). • Psychosocially, mentally and physically able to fully comply with this protocol including adhering to follow-up schedule and requirements and filling out of forms. • Signed informed consent.	• No more than 2 vertebral levels may have DDD and all diseased levels must be treated • Subjects with involved vertebral endplates dimensionally smaller than 34.5 mm in the medial-lateral and/or 27 mm in the anterior-posterior directions • Known allergy to titanium, polyethylene, cobalt, chromium or molybdenum • Prior fusion surgery at any vertebral level (limited to prior lumbar fusion surgery) • Clinically compromised vertebral bodies at the affected level(s) due to current or past trauma • Radiographic confirmation of facet joint disease or degeneration • Lytic spondylolisthesis or spinal stenosis • Degenerative spondylolisthesis of grade > 1 • Back or leg pain of unknown etiology • Osteoporosis: A screening questionnaire for osteoporosis, SCORE (Simple • Calculated Osteoporosis Risk Estimation), used to screen subjects who require a DEXA bone mineral density measurement. If DEXA was required, exclusion was defined as a DEXA bone density measured T score ≤ -2.5 (The World Health Organization definition of osteoporosis.) • Paget's disease, osteomalacia or any other metabolic bone disease (excluding osteoporosis which is addressed above) • Morbid obesity defined as a body mass index > 40 or a weight more than 100 lbs. over ideal body weight • Pregnant or interested in becoming pregnant in the next 3 years. • Active infection - systemic or local • Taking medications or any drug known to potentially interfere with bone/soft tissue healing (e.g., steroids) • Rheumatoid arthritis or other autoimmune disease • Systemic disease including AIDS, HIV, Hepatitis • Active malignancy: A subject with a history of any invasive malignancy (except non- melanoma skin cancer), unless he/she had been treated with curative intent and there had been no clinical signs or symptoms of the malignancy for at least 5 years.

2. Follow-Up Schedule

Table 6: Follow-up Schedule

Visit	Background Data & Medical History	Physical & Neurological Exam	DEXA	Confirm DDD	A/P & Lateral Films	Flexion Extension and Lateral Bending Films	Subject Self-Assessment
Enrollment / Pre-operative	X	X	A	B	X	X	C
Post-op/ Prior to Discharge					D		
6 wk. (+/- 2 wk.)		X			X	F	E
3 mo. (+/- 2 wk.)		X			X	F	E
6 mo. (+/-1mo)		X			X	X	E
12 mo. (+/-2 mo.)		X			X	X	E
18 mo. (+/-2mo)		X			X	X	E
24 months (+/-2 mo.)		X			X	X	E
Annually thereafter (+/-2 mo.)		X			X	X	E

A. DEXA bone mineral density was recorded when dictated by osteoporosis screening (SCORE).
B. In accordance with the definition of DDD, disc pathology was confirmed by MRI, CT, discography, plain film, myelography and/or flexion /extension films. All clinical imaging used in the confirmation of DDD must have been taken at this visit or within the last 6 months.
C. Subject completed self-assessment tools: pain (VAS); Oswestry Questionnaire (ODI); and SF-36.
D. A/P and lateral films were taken early post-op and/or prior to hospital discharge.
E. Subject completed self-assessment tools: pain (VAS); satisfaction (VAS); Oswestry Questionnaire (ODI); and SF-36.
F. Flexion–extension films and lateral bending films were taken at this visit for pro**disc**® L recipients and were taken for fusion subjects whenever possible and clinically advisable (i.e., at the surgeon's clinical discretion).

3. Clinical Endpoints

The protocol specified that the primary endpoints were based on the Month 24 visit, with the exception of re-operations that were cumulative from index surgery through Month 24 post-operative. Treatment success was defined in the protocol using a composite endpoint for safety and effectiveness as follows:

An individual subject's pro**disc**® L implantation was considered successful, if and only if, all of the following criteria were met:

ODI:	Improvement of 15% at 24 months compared to the baseline value
Re-operation:	No re-operation required to remove or modify the pro**disc**® L implant (investigational group) or to modify the fusion site or correct a complication with an implant (control group)
Short Form (SF-36)	Improvement compared to Baseline (24-month score-Baseline score > 0)
Neurologic status:	Neurologic status improved or maintained in motor, sensory, reflex, and straight leg-raise tests
Radiographic success:	• No radiographic evidence of device migration or subsidence (>3mm)

- No extensive radiolucency along the implant/bone interface (< 25% of interface's length for each endplate)
- ROM at the implanted level was maintained or improved from the pre-operative baseline*
- No loss of disc height (> 3 mm)
- No evidence of bony fusion in investigational group

*ROM at the implanted level maintained or improved if the flexion/extension ROM at 24 months was maintained from baseline measurement (with ± 3° measurement error applied)

The margin for establishing non-inferiority was 12.5%.

A control subject's fusion surgery was considered successful, if and only if all of the following criteria were met:

ODI:	Improvement of 15% over the baseline value
Re-operation:	No re-operation required to modify the fusion site or correct a complication with an implant
Short Form (SF-36)	Improvement compared to baseline
Neurologic status:	Neurologic status improved or maintained in motor, sensory, reflex, and straight leg-raise tests
Radiographic success:	• Strong evidence of fusion including > 50% trabecular bridging or bone mass maturation and increased or maintained bone density at the interbody fusion site; • No motion (defined as translation >3 mm and angulation >5° on flexion-extension films:); • No visible gaps in the fusion mass; • No loss of disc height (> 3mm); • No migration and subsidence of implants (> 3mm) • No implant loosening (no halos/radiolucencies around the implant).

The protocol considered the study a success if at 24 months the overall success rate of the investigational group was not inferior to that of the overall success rate of the control group; and the device related complication rate (including subsequent surgical interventions and

neurological complications) of the investigational group was not inferior to that of the control group. The margin for establishing non-inferiority was stated in the protocol as 12.5%.

As part of its review of the PMA Supplement for two-level implantation for pro**disc**® L, FDA requested analysis of a revised endpoint. This FDA-requested endpoint was similar to the protocol-defined endpoint described above but utilized a 15-point improvement in ODI as well as the radiographic success defined below. The FDA-requested endpoints required a margin for establishing non-inferiority of 10%. In addition, in part due to the lack of validated values for "ideal" ROM in the lumbar spine, a correlation between ROM and clinical success had not been demonstrated at the time of this PMA Supplement. As a result, an assessment of the FDA-requested overall success without the range of motion component was also utilized. The results from these FDA-requested endpoints (with and without ROM) are the ones presented in this document.

The FDA-requested primary endpoints include:

ODI:	Improvement of ≥ 15 points at 24 months compared to baseline
Re-operation:	No re-operation required to remove or modify the pro**disc**® L implant (investigational group) or to modify the fusion site or correct a complication with an implant (control group)
Short Form (SF-36)	Improvement compared to Baseline (24-month score-Baseline score > 0)
Neurologic status:	Improved or maintained in motor, sensory, reflex, and straight leg-raise tests
Radiographic success:	a. No radiographic evidence of device migration or subsidence (>3mm) b. No extensive radiolucency along the implant/bone interface or implant loosening (< 25% of interface length at each endplate for implant group, and no halos or radiolucencies around the implant in the control group) c. No loss of disc height (> 3 mm) d. No evidence of bony fusion in investigational group; strong evidence of fusion in control (>50% trabecular bridging bone or bone mass maturation and increased or maintained bone density at the interbody fusion site) with no visible gaps in the fusion mass e. ROM at implanted level maintained or improved from pre-operative baseline in investigational group and no motion on flexion/extension films (defined as < 3mm translation and < 5° angulation) in the control group

The margin for establishing non-inferiority was 10%.

Secondary endpoints are expected to further define the safety and effectiveness of pro**disc**® L Total Disc Replacement for the implantation at two adjacent vertebral levels.

Secondary endpoints included:

- Back and Leg Pain as assessed using the Visual Analog Scale (VAS)
- Health-Related Quality of Life (SF-36)
- Subject Satisfaction as assessed using the Visual Analog Scale (VAS)
- Subject Satisfaction as assessed by the question: "Would you have the surgery again?"
- Pain management medication (medication use)
- Peri- and intra-operative data (operative time, blood loss, hospital stay length)
- Return to Work
- Physical Labor
- Adverse Events
- Adjacent level analysis (surgical interventions at the adjacent level, non-surgical AEs, and radiographic analysis)

Clinical Events Committee (CEC)

A Clinical Events Committee (CEC) was convened after completion of the study to review and adjudicate adverse event determinations. The CEC consisted of two independent spine surgeons. The CEC members had no financial interest with the sponsor and had prior experience implanting and treating patients with lumbar total disc replacement devices.

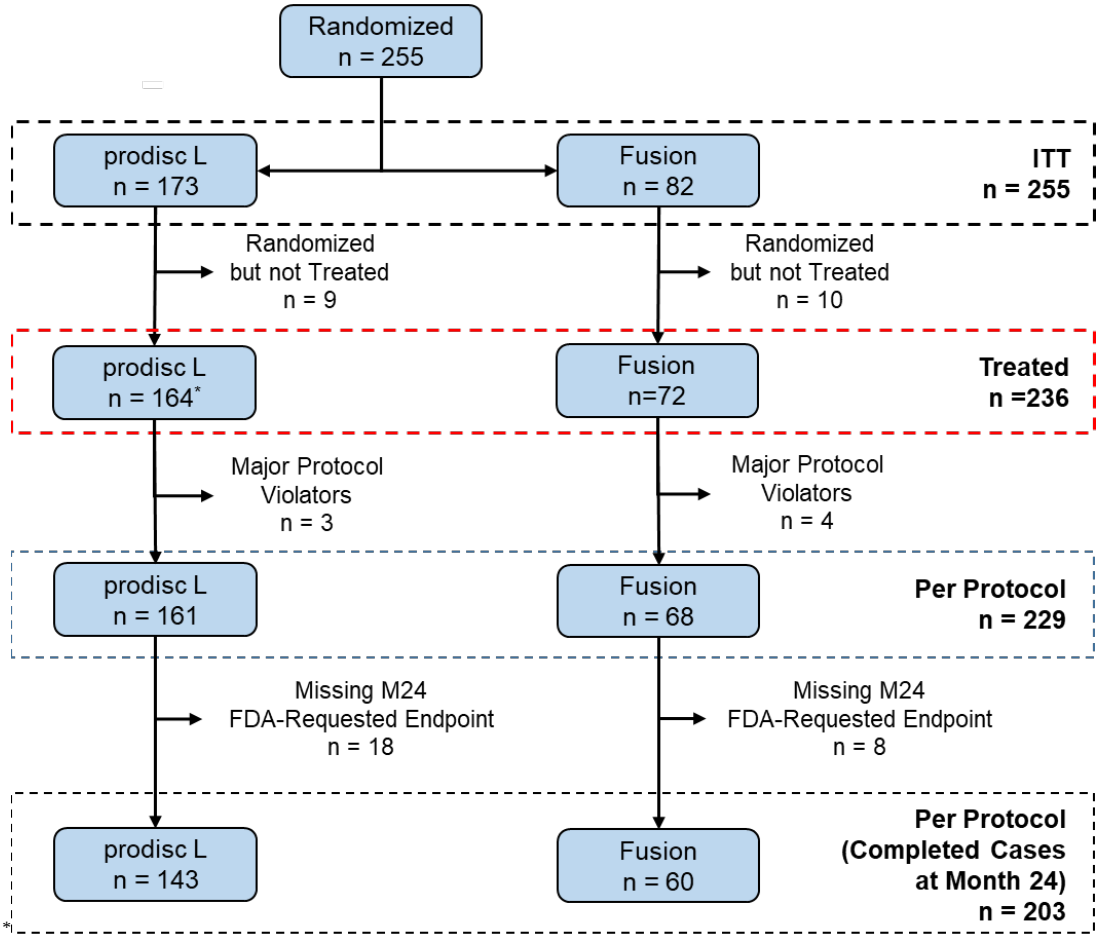
The CEC reviewed all adverse events. For each AE, the CEC indicated either agreement or disagreement with the original designations that were made by the investigator (for implant relatedness, surgery relatedness, and severity) or sponsor (for severe/life-threatening status and AE category). The CEC adjudicated all adverse events such that unanimous agreement was required for all decisions to agree or disagree/revise a prior designation. The CEC-adjudicated AE designations were used as a basis for the results reported in the safety section of this document.

B. Accountability of PMA Cohort

Detailed pre-operative demographic information was collected for all subjects entering the study. Subjects who met all inclusion/exclusion criteria were asked to enroll in the study. Subjects who agreed to participate in the study then signed the informed consent forms prior to being randomized. After the subject signed the informed consent form, the surgeon notified the sponsor to obtain the subject's treatment assignment.

In this study, the first pro**disc**® L two-level implantation occurred on January 10, 2002. Enrollment in the randomized cohort closed on June 23, 2004. This study required a 24 Month follow-up period.

The analysis populations for this study are defined below. A schematic showing subject flow for these analysis populations at Month 24 is included as Figure 2.



*One pro**disc**® L subject was surgically enrolled in the investigational arm without the use of the randomization sequence. This subject was excluded from the ITT cohort and this accounting tree but was included in the safety analysis of the treated subjects, for n=165 pro**disc**® L subjects in the safety analysis.

Figure 2: Subject Accounting Tree

The *Intent to Treat (ITT)* population included every subject randomized according to randomized treatment assignment. The *Treated* population included all subjects who were enrolled and treated. There were 236 subjects in the *Treated* population (n=72, Fusion; n= 164, pro**disc**® L). The demographic and safety analyses utilized the *Treated* population, with the addition of one pro**disc**® L subject who was surgically enrolled in the investigational arm without the use of the randomization sequence (n=72, Fusion; n= 165, pro**disc**® L). This single subject was excluded from the ITT population due to not being formally randomized.

According to the ICH Guidelines for Statistical Principles for Clinical Trials (E9), the use of an intent-to-treat population in equivalence or non-inferiority trials is generally not conservative. Therefore, the study hypothesis (i.e., overall success) was evaluated using the *Per Protocol* population. The *Per Protocol* population included all subjects who were enrolled and treated on protocol and excludes Major Protocol Violators (MPVs). There were 229 subjects (n=68, Fusion and 161 pro**disc**® L) in the *Per Protocol* population.

Subjects were followed to Month 60. Definitions are provided below for each of the categories contained in the Subject Accountability Table (Table 7). The database was closed June 29, 2012 and locked on November 20, 2012.

Table 7: Subject Accounting and Follow-up Compliance Table for Outcomes

	Month 24				Month 60			
	prodisc® L		Fusion		prodisc® L		Fusion	
	n	%	n	%	n	%	n	%
ITT Cohort	**173**	--	**82**	--	**173**	--	**82**	--
Not Treated	*9*	--	*10*	--	*9*	--	*10*	--
Major Protocol Violations	*3*	--	*4*	--	*3*	--	*4*	--
Per Protocol Cohort	**161**	--	**68**	--	**161**	--	**68**	--
Deaths	*2*	--	*0*	--	*2*	--	*1*	--
Not Yet Overdue/Not Yet Due	*0*	--	*0*	--	*0*	--	*0*	--
Expected Due	**159**	--	**68**	--	**159**	--	**67***	--
Overall Success Evaluation								
• Overall Success Evaluation (FDA requested)	143	89.9%	60	88.2%	127	79.9%	57	83.8%
• Overall Success Evaluation (FDA requested, no ROM)	143	89.9%	60	88.2%	126	79.2%	57	83.8%
Clinical Evaluation								
• Neurological Evaluation	142	89.3%	61	89.7%	125	78.6%	53	79.1%
• Oswestry Disability Index Evaluation	143	89.9%	61	89.7%	125	78.6%	53	79.1%
• SF-36 Evaluation	142	89.3%	58	85.3%	123	77.4%	52	77.6%
• VAS Low Back and Leg Pain Evaluation	142	89.3%	61	89.7%	124	78.0%	53	79.1%
Radiographic Evaluation								
• Range of Motion Evaluation	131	82.4%	60	88.2%	118	74.2%	51	76.1%
• Bridging Bone Evaluation	141	88.7%	60	88.2%	120	75.5%	51	76.1%
• Disc Height Evaluation	135	84.9%	57	83.8%	119	74.8%	51	76.1%
• Migration Evaluation	141	88.7%	60	88.2%	120	75.5%	51	76.1%
• Radiolucency Evaluation	141	88.7%	60	88.2%	120	75.5%	51	76.1%
• Subsidence Evaluation	141	88.7%	60	88.2%	120	75.5%	51	76.1%

*One Fusion subject died in the Month 60 timeframe, but previously had a surgical intervention. As such, this subject was included in the expected due for overall success measurements, but not for clinical and radiographic evaluation.

C. Study Population Demographics and Baseline Parameters

Detailed preoperative demographic information was collected for all subjects entering the study. The demographics of the study population are typical for a total-disc replacement study performed in the US.

Pre-operative data for Fusion, and pro**disc**® L subjects in the treated population are presented in Table 8, including: age, gender, race, smoking status, height, weight, body mass index (BMI), Oswestry score, percentage pain in the back versus leg, and duration of pain in the back/leg. The mean age demographic profile for the treated subjects (Fusion and pro**disc**® L) was 41.8 years of age. The demographic profiles of the Fusion and pro**disc**® L subjects for all categories were not statistically different.

Table 8: Pre-Operative Demographic Profile for Fusion and prodisc® L

	prodisc® L n = 164	Fusion n = 72	p- value*
Age at Surgery (Years)			**0.955**
Mean (STD)	41.8 (7.75)	41.8 (7.81)	
Range	22 - 60	22 - 58	
Age Group			**0.889**
<= 42 Years	86 (52.4%)	37 (51.4%)	
> 42 Years	78 (47.6%)	35 (48.6%)	
Total	164 (100%)	72 (100%)	
Gender			**0.671**
Female	70 (42.7%)	33 (45.8%)	
Male	94 (57.3%)	39 (54.2%)	
Total	164 (100%)	72 (100%)	
Race			**0.387**
Caucasian	144 (87.8%)	66 (91.7%)	
African American	2 (1.2%)	2 (2.8%)	
Hispanic	13 (7.9%)	3 (4.2%)	
Asian	1 (0.6%)	1 (1.4%)	
Other	4 (2.4%)	0 (0.0%)	
Total	164 (100%)	72 (100%)	
Smoking Status			**0.208**
Never	85 (52.1%)	29 (40.3%)	
Former	31 (19.0%)	21 (29.2%)	
Current	47 (28.9%)	22 (30.6%)	
Total	163 (100%)	72 (100%)	
Height (in)			**0.952**
Mean (STD)	68.30 (4.20)	68.3 (3.71)	
Range	58 - 78	60 - 80	
Weight (lbs.)			**0.819**
Mean (STD)	180.36 (39.42)	180.9 (35.88)	
Range	98 - 285	111 - 285	
Body Mass Index (Kg/m^2)			**0.915**
Mean (STD)	27.07 (4.52)	27.1 (4.05)	
Range	17.96 - 38.92	19.2 - 37.4	
Oswestry Disability Index			**0.845**
Mean (STD)	64.70 (11.42)	64.8 (9.54)	
Range	40.0 – 98.0	44.0 – 82.0	
Percent Pain in the Back versus Leg			**0.094**
100%/0%	50 (30.5%)	21 (30.0%)	
75%/25%	95 (57.9%)	36 (51.4%)	
50%/50%	19 (11.6%)	13 (18.6%)	
25%/75%	0 (0.0%)	0 (0.0%)	
0%/100%	0 (0.0%)	0 (0.0%)	
Total	164 (100%)	70 (1%)	
Duration of Pain in the Back/Leg			**0.530**
< 6 Months	1 (0.6%)	0 (0.0%)	
6 Months To 1 Year	16 (9.8%)	4 (5.6%)	
> 1 Year	147 (89.6%)	68 (94.4%)	
Total	164 (100%)	72 (100%)	

*Continuous and ordinal variables were analyzed by a two-sided Wilcoxon rank sum test, and categorical variables were analyzed using a two-sided Fisher's exact test to compare Fusion and pro**disc**® L.

Table 9 summarizes the available pre-operative data related to the radiographic inclusion criteria for the treated population.

Table 9: Radiographic Findings Reported at the Pre-Operative Visit

	prodisc® L		Fusion	
	Cranial	**Caudal**	**Cranial**	**Caudal**
Satisfied inclusion criteria for DDD	164/164 (100%)	164/164 (100%)	72/ 72 (100%)	72/ 72 (100%)
Exclusion Criteria: ≤ Grade I	0/164 (0.0%)	0/164 (0.0%)	0/ 72 (0.0%)	0/ 72 (0.0%)
Additional pre-operative radiographic findings:				
Scarring/thickening of annulus fibrosis	59/158 (37.3%)	61/156 (39.1%)	19/ 64 (29.7%)	21/ 64 (32.8%)
Herniated nucleus pulposus	47/158 (29.7%)	56/156 (35.9%)	22/ 64 (34.4%)	25/ 65 (38.5%)
Vacuum phenomenon	18/159 (11.3%)	38/158 (24.1%)	4/ 64 (6.3%)	12/ 64 (18.8%)
Grade I spondylolisthesis	0/158 (0.0%)	0/157 (0.0%)	0/ 64 (0.0%)	0/ 65 (0.0%)
≥5° angulation (flexion-extension)	76/159 (47.8%)	78/155 (50.3%)	39/ 68 (57.4%)	41/ 67 (61.2%)

Information regarding pre-operative medical treatment in the treated population is presented in Table 10.

Table 10: Pre-Operative Treatment for Fusion and prodisc® L

	prodisc® L n = 164	**Fusion n = 72**
Prior Treatment* (Other Than Medication		
Injection	126 (76.8%)	52 (72.2%)
Physical Therapy	135 (82.3%)	61 (84.7%)
Corset/Brace	68 (41.5%)	28 (38.9%)
Chiropractic	59 (36.0%)	28 (38.9%)
Other	34 (20.7%)	12 (16.7%)
Prior Surgical Treatment*		
None	96 (58.5%)	43 (59.7%)
Any Prior Surgery	68 (41.5%)	30 (41.1%)
Discectomy	31 (18.9%)	13 (18.1%)
IDET**	16 (9.8%)	7 (9.7%)
Laminectomy	31 (18.9%)	9 (12.5%)
Laminotomy	4 (2.4%)	2 (2.8%)
Other	12 (7.3%)	8 (11.1%)

* Subjects may be included in more than one category. Number of subjects treated was used as the denominator to compute all percentages.
** Intradiscal Electrothermoplasty

Selected intra-operative and discharge results for subjects in the treated population are presented in Table 11. Table 12 summarizes the distribution of device component sizes utilized in the study for pro**disc**® L subjects in the treated population.

The mean intra-operative time was significantly shorter in thepro**disc**® L group compared to the Fusion group ($p < 0.001$). The estimated blood loss was significantly less in the pro**disc**® L group compared to the Fusion group ($p < 0.001$). The length of hospital stay was also significantly shorter in the pro**disc**® L group compared to the Fusion group ($p < 0.001$).

There were 14 subjects with intra-operative blood loss >1500 mL (6 Fusion [8.3%] and 8 pro**disc**® L [4.9%]). The incidence rate between Fusion and pro**disc**® L was not significant ($p = 0.3719$).

Table 11: Intra-operative and Discharge Summary Statistics

	prodisc® L (n = 164)	**Fusion (n = 72)**	**p-value***
Levels Treated			**0.460**
L3-L5	13 (7.9%)	7 (9.7%)	
L4-S1	150 (91.5%)	64 (88.9%)	
Other (1- or 3-level)	1 (0.6%)	1 (1.4%)	
Intra-Operative Time (Minutes)			**<0.001**
N	164	72	
Mean (STD)	159.3 (72.64)	272.8 (81.68)	
Range	66 – 430	86 - 515	
Estimated Blood Loss (cc)			**<0.001**
N	161	72	
Mean (STD)	398.7 (452.82)	549.3 (466.63)	
Range	0 – 3000	0 - 2000	
Intra-Operative Antibiotics			**0.863**
Yes	130 (79.3%)	56 (77.8%)	
No	34 (20.7%)	16 (22.2%)	
Total	164 (100%)	72 (100%)	
DVT Prophylaxis**			**N/A**
None	0 (0.0%)	0 (0.0%)	
TED Hose	147 (89.6%)	65 (90.3%)	
SCD	81 (49.4%)	38 (52.8%)	
Other	6 (3.7%)	4 (5.6%)	
Length of Hospital Stay (days)			**<0.001**
N	164	72	
Mean (STD)	3.8 (1.53)	5.0 (1.93)	
Range	1 – 10	2 - 14	

*Continuous and ordinal variables were analyzed by a Wilcoxon rank sum test, and categorical variables were analyzed using Fisher's exact test to compare Fusion to pro**disc**® L.
** Subjects may be included in more than one category. Number of subjects treated used as the denominator to compute all percentages.

Table 12: Distribution of prodisc® L Sizes

Size	Angle	Polyethylene Height	prodisc® L
Medium	6 degrees	10 mm	159 (49.1%)
		12 mm	24 (7.4%)
		14 mm	1 (0.3%)
	11 degrees	10 mm	44 (13.6%)
		12 mm	6 (1.9%)
		14 mm	1 (0.3%)
Large	6 degrees	10 mm	51 (15.7%)
		12 mm	19 (5.9%)
		14 mm	2 (0.6%)
	11 degrees	10 mm	11 (3.4%)
		12 mm	6 (1.9%)
		14 mm	0 (0.0%)
Total number of devices			**326 (100%)**

D. Safety and Effectiveness Results

1. Safety Results

The safety analysis cohort (Figure 2) consisted of all subjects randomized and treated plus one pro**disc**® L subject who received the treatment without randomization (n=72, Fusion; n= 165, pro**disc**® L). All adverse events available up to 5-years follow-up were reported. The key safety findings and adverse events are reported in Tables 13 to 25.

Table 13: Comparisons of Summary Adverse Event Rates between prodisc® L and Fusion Groups

	prodisc® L (n=165)			Fusion (n=72)			Dif	Exact
	Events	Subjs	%*	Events	Subjs	%*	%*	p[1]
Any adverse event	**1058**	**153**	**92.7%**	**536**	**70**	**97.2%**	**-4.5%**	**0.238**
Any device or surgery-related adverse event	**265**	**99**	**60.0%**	**162**	**49**	**68.1%**	**-8.1%**	**0.248**
Device-related adverse event	2	2	1.2%	2	2	2.8%	-1.6%	0.587
Surgery-related adverse event	264	98	59.4%	161	48	66.7%	-7.3%	0.312
Any severe or life-threatening adverse event	**65**	**41**	**24.8%**	**42**	**26**	**36.1%**	**-11.3%**	**0.086**
Any device or surgery-related severe or life-threatening adverse event	**16**	**13**	**7.9%**	**21**	**16**	**22.2%**	**-14.3%**	**0.004**
Device-related severe or life-threatening adverse event	1	1	0.6%	0	0	0.0%	0.6%	1.000
Surgery-related severe or life-threatening adverse event	15	12	7.3%	21	16	22.2%	-14.9%	0.002
Deaths	**2**	**2**	**1.2%**	**1**	**1**	**1.4%**	**-0.2%**	**1.000**

*Percentage of subjects experiencing specific event without regard to length of follow-up.
[1]Two-sided Fisher's Exact test.

As seen in Table 13, there was not a statistically significant difference in the total adverse event rate between the pro**disc**® L and Fusion groups. However, compared to the Fusion subjects, the pro**disc**® L subjects exhibited a lower overall rate of any severe or life-threatening adverse events (24.8 vs. 36.1%) and any device or surgery related severe or life-threatening adverse events (7.9 vs. 22.2%). It should be noted that the only device-related severe or life-threatening adverse

event occurred in the pro**disc**® L group. These lower adverse event rates were statistically significant. This statistically significant difference was attributed to the nature of the therapeutic interventions in each cohort.

A more detailed description of the adverse event categorizations utilized in this study are described in Table 14.

Table 14: Adverse Event Categories

CATEGORY	DEFINITION
PAIN – BACK AND LOWER EXTREMITY	
pain – back	pain (including ache, stiffness, strain, sensitivity or throbbing) limited to the back and pelvis.
pain - back and lower extremities	pain (including ache, stiffness, strain, sensitivity or throbbing) involving the back and lower extremities; excluding cases with burning sensation.
pain - back and lower extremities with burning	pain (including ache, stiffness, strain, sensitivity or throbbing) involving the back and lower extremities combined with tingling / burning in the lower leg.
pain - back and lower extremities with numbness at index level	pain (including ache, stiffness, strain, sensitivity or throbbing) involving the back and lower extremities combined with numbness or tingling within the distribution of nerves at the index level.
pain - back and other	pain (including ache, stiffness, strain, sensitivity or throbbing) of the back combined with pain in another area of the body (e.g., neck, chest and pelvis).
pain - groin area	pain limited to the groin area
pain - lower extremities	pain (including ache, stiffness, strain, sensitivity or throbbing) involving the lower extremities.
pain - lower extremities with numbness at index level	pain (including ache, stiffness, strain, sensitivity or throbbing) involving the lower extremities combined with numbness or tingling within the distribution of nerves at the index level.
NEUROLOGICAL	
motor deficit in index level	any condition relating to a motor deficit at the spinal level of the index treatment.
nerve root injury	a condition with symptoms of nerve root injury.
numbness index level related	numbness or tingling within the distribution of nerves at the index level.
numbness peripheral nerve or non-index level related	numbness or tingling outside the distribution of nerves at the index level.
reflex change	a change in reflex.
retrograde ejaculation	retrograde ejaculation
DEGENERATIVE DISEASE PROGRESSION	
degenerative disease progression, non-lumbar	new signs or symptoms of spinal degeneration outside the lumbar spine
degenerative disease progression, other lumbar	new signs or symptoms of spinal degeneration of the lumbar spine, excluding herniated nucleus pulposus.
herniated nucleus pulposus	a herniation of the nucleus pulposus intervertebral disc, distant from the index level.
herniated nucleus pulposus, adjacent level	a herniation of the nucleus pulposus intervertebral disc, adjacent to the index level.
ADDITIONAL SURGERY INDEX LEVEL	
migration requiring surgery	post-op radiographs indicate that the implant may have changed positions in a direction parallel to the vertebral endplate and this led to further surgery.
surgery - index level (other)	a surgical procedure at the same level of the lumbar spine as the index procedure performed subsequent to the index procedure which did not involve removal or modification of the implant or implantation of additional instrumentation.

CATEGORY	DEFINITION
surgery - index level (revision)	a surgical procedure at the same level of the lumbar spine as the index procedure performed subsequent to the index procedure which involved modification of the implant or removal of any part of the implant (with or without replacement).
surgery - index level (supplemental fixation)	a surgical procedure at the same level of the lumbar spine as the index procedure performed subsequent to the index procedure which involved implantation of additional instrumentation at the index level.
INCISION SITE RELATED	
infection - superficial wound with incision site pain	an infection near the surface of the surgical incision.
pain - incision site	pain limited to the area of the surgical incision(s) including the graft site.
wound issues, other	a condition pertaining to the surgical or other wound that did not involve infection.
INFECTION, NOT INDEX LEVEL RELATED	
infection - other non-wound related	an infection in an area other than the surgical incision (except urinary tract infections)
infection - uti	an infection in the urinary system.
pulmonary infection	an infection of the pulmonary system or symptoms consistent with a pulmonary infection (e.g., bronchitis)
MUSCULOSKELETAL SPASMS	
musculoskeletal spasms - back	a condition involving sudden contraction of muscles limited to the back or pelvis.
musculoskeletal spasms - back and leg	a condition involving sudden contraction of muscles involving both the back and lower extremities.
musculoskeletal spasms - leg	a condition involving sudden contraction of muscles limited to the legs.
non-specific musculoskeletal spasms	a condition involving sudden contraction of muscles without identification of specific muscles or regions affected.
DERMATOLOGICAL OR DRUG ALLERGY	
dermatological	any condition pertaining to the skin other than drug allergies or surgical wound site.
dermatological drug allergy	any condition pertaining to the skin associated with drug allergies.
drug allergy	any condition associated with abnormal immune system reaction to a medication (other than dermatological drug allergies)
pruritus	itching or rash
VASCULAR INJURY	
clinically significant blood loss (>1500 cc)	blood loss > 1500 cc without corresponding notation of physical injury to a blood vessel
vessel damage/bleeding, major	physical injury to a blood vessel resulting in blood loss > 1500 cc.
vessel damage/bleeding, minor	physical injury to a blood vessel resulting in blood loss up to 1500 cc.
OTHER	
anemia	a decrease in red blood cell count evidenced by diagnosis, lab test results, or treatment with a blood transfusion.
burning or dysesthetic pain	dysesthesia in the back, or lower extremities or surgical site.
cardiovascular	any condition of the heart and/or blood vessels (excluding the blood vessels that supply the brain).
death	termination of life.
dizziness	a condition described as feeling faint, lightheaded or unsteady.
dural tear	a tear of the dura with or without evidence of spinal fluid leakage
edema	swelling of tissues.
fatigue	a feeling of tiredness.
fever	diagnosis of fever or elevated temperature.
fracture (non-vertebral)	a break in the continuity of the bone (excluding the spinal vertebra).

CATEGORY	DEFINITION
gastrointestinal	any condition pertaining to the stomach and intestines.
genitourinary	any condition pertaining to the reproductive or urinary systems (except infections of the urinary system).
headache	pain in various parts of the head.
hernia	a hernia in the abdominal region.
incontinence	involuntary leakage of urine or fecal matter.
insomnia	a sleep disorder in which there is an inability to fall asleep or to remain asleep as long as desired.
migration not requiring surgery	post-op radiographs indicate that the implant may have changed positions in a direction parallel to the vertebral endplate; however, this did not lead to further surgery.
narcotics use	a diagnosis or other report indicating drug dependency or addiction.
other	an adverse event not associated with any other term.
other musculoskeletal	any condition pertaining to the muscles or skeleton excluding those under more specific terms
pain other (not back/hip/leg)	pain not associated with any other term.
psychological	any psychological condition
radiolucency - graft	radiographic appearance of radiolucency without clinical symptoms.
respiratory	a condition pertaining to the respiratory system; excluding pulmonary infections
subsidence not requiring surgery	post-op radiographs indicate that the implant may have subsided into the vertebral endplate; however, this did not lead to further surgery.
surgery - adjacent level	a surgical procedure on the lumbar spine at a different level of the spine than the index procedure and performed subsequent to the index procedure.
surgery - other	a surgical procedure that did not involve treatment of degenerative disc disease of the lumbar spine, this includes spinal and non-spinal surgeries
thrombosis	a condition involving symptoms of thrombosis
thrombosis (dvt leg)	a condition involving a diagnosis of deep vein thrombosis
vertebral fracture	a break in the continuity of the bone of the spinal vertebra.

Table 15 presents the incidence of adverse events, the number of events, and the events reported per subject in both pro**disc**® L (n=153 total adverse events, n=165 subjects) and Fusion (n=70 total adverse events, n=72 subjects) groups. The rates of adverse events are summarized by category and subcategory.

Table 15: Counts and Percentages of Subjects with Specific Adverse Event Categories

All Adverse Events	prodisc® L			Fusion			Dif	Exact
	Events	Subjs	%*	Events	Subjs	%*	%*	p[1]
ALL	**1058**	**153**	**92.7%**	**536**	**70**	**97.2%**	**-4.5%**	**0.238**
PAIN - BACK AND LOWER EXTREMITY	**288**	**121**	**73.3%**	**148**	**63**	**87.5%**	**-14.2%**	**0.017**
pain - back	97	67	40.6%	55	42	58.3%	-17.7%	0.016
pain - back and lower extremities	63	46	27.9%	27	23	31.9%	-4.1%	0.537
pain - back and lower extremities with burning	3	3	1.8%	2	1	1.4%	0.4%	1.000
pain - back and lower extremities with numbness at index level	9	8	4.8%	3	3	4.2%	0.7%	1.000
pain - back and other	15	15	9.1%	5	5	6.9%	2.1%	0.800
pain - groin area	7	7	4.2%	3	2	2.8%	1.5%	0.726
pain - lower extremities	83	61	37.0%	43	30	41.7%	-4.7%	0.562
pain - lower extremities and incision site	1	1	0.6%	1	1	1.4%	-0.8%	0.516
pain - lower extremities with numbness at index level	10	8	4.8%	9	6	8.3%	-3.5%	0.369

All Adverse Events	prodisc® L			Fusion			Dif	Exact
	Events	Subjs	%*	Events	Subjs	%*	%*	p[1]
NEUROLOGICAL EVENTS	**58**	**39**	**23.6%**	**28**	**19**	**26.4%**	**-2.8%**	**0.743**
motor deficit in index level	5	5	3.0%	1	1	1.4%	1.6%	0.670
neurological	5	4	2.4%	2	2	2.8%	-0.4%	1.000
numbness index level related	5	5	3.0%	4	3	4.2%	-1.1%	0.702
numbness peripheral nerve or non-index level related	43	31	18.8%	20	15	20.8%	-2.0%	0.723
reflex change	0	0	0.0%	1	1	1.4%	-1.4%	0.304
DEGENERATIVE DISEASE PROGRESSION	**15**	**12**	**7.3%**	**9**	**8**	**11.1%**	**-3.8%**	**0.322**
degenerative disease progression, non-lumbar	7	7	4.2%	1	1	1.4%	2.9%	0.441
degenerative disease progression, other lumbar	7	6	3.6%	8	7	9.7%	-6.1%	0.069
herniated nucleus pulposus	1	1	0.6%	0	0	0.0%	0.6%	1.000
ADDITIONAL SURGERY INDEX LEVEL	**5**	**5**	**3.0%**	**14**	**12**	**16.7%**	**-13.6%**	**<.001**
migration requiring surgery	1	1	0.6%	0	0	0.0%	0.6%	1.000
surgery - index level (other)	3	3	1.8%	0	0	0.0%	1.8%	0.555
surgery - index level (revision)	0	0	0.0%	14	12	16.7%	-16.7%	<.001
surgery - index level (supplemental fixation)	1	1	0.6%	0	0	0.0%	0.6%	1.000
INCISION SITE RELATED	**42**	**36**	**21.8%**	**23**	**20**	**27.8%**	**-6.0%**	**0.324**
infection - superficial wound with incision site pain	6	6	3.6%	6	6	8.3%	-4.7%	0.194
pain - incision site	19	19	11.5%	9	8	11.1%	0.4%	1.000
wound issues, other	17	15	9.1%	8	7	9.7%	-0.6%	1.000
INFECTION, NOT INDEX LEVEL RELATED	**20**	**15**	**9.1%**	**7**	**7**	**9.7%**	**-0.6%**	**1.000**
infection - other non-wound related	14	13	7.9%	4	4	5.6%	2.3%	0.597
infection - uti	4	4	2.4%	2	2	2.8%	-0.4%	1.000
pulmonary infection	2	2	1.2%	1	1	1.4%	-0.2%	1.000
MUSCULOSKELETAL SPASMS	**49**	**34**	**20.6%**	**15**	**12**	**16.7%**	**3.9%**	**0.593**
musculoskeletal spasms - back	24	21	12.7%	9	9	12.5%	0.2%	1.000
musculoskeletal spasms - back and leg	5	5	3.0%	1	1	1.4%	1.6%	0.670
musculoskeletal spasms - leg	10	9	5.5%	3	3	4.2%	1.3%	1.000
non-specific musculoskeletal spasms	10	8	4.8%	2	2	2.8%	2.1%	0.728
DERMATOLOGICAL OR DRUG ALLERGY	**20**	**16**	**9.7%**	**16**	**11**	**15.3%**	**-5.6%**	**0.266**
dermatological	8	5	3.0%	8	6	8.3%	-5.3%	0.094
drug allergy/reaction	2	2	1.2%	3	3	4.2%	-3.0%	0.166
pruritus	10	10	6.1%	5	4	5.6%	0.5%	1.000
VASCULAR INJURY	**10**	**10**	**6.1%**	**7**	**7**	**9.7%**	**-3.7%**	**0.411**
clinically significant blood loss (>1500 cc)	6	6	3.6%	6	6	8.3%	-4.7%	0.194
vessel damage/bleeding, major	2	2	1.2%	1	1	1.4%	-0.2%	1.000
vessel damage/bleeding, minor	2	2	1.2%	0	0	0.0%	1.2%	1.000
OTHER	**551**	**135**	**81.8%**	**270**	**58**	**80.6%**	**1.3%**	**0.857**
anemia	11	11	6.7%	15	11	15.3%	-8.6%	0.050
bowel perforation	1	1	0.6%	0	0	0.0%	0.6%	1.000
burning or dysesthetic pain	10	10	6.1%	3	2	2.8%	3.3%	0.355
cardiovascular	20	17	10.3%	11	7	9.7%	0.6%	1.000
death	2	2	1.2%	1	1	1.4%	-0.2%	1.000
dizziness	7	7	4.2%	4	4	5.6%	-1.3%	0.739
dural tear	1	1	0.6%	3	3	4.2%	-3.6%	0.085
edema	15	12	7.3%	8	8	11.1%	-3.8%	0.322
fatigue	1	1	0.6%	2	2	2.8%	-2.2%	0.220
fever	32	31	18.8%	15	13	18.1%	0.7%	1.000
fracture (non-vertebral)	6	6	3.6%	3	3	4.2%	-0.5%	1.000
gastrointestinal	98	67	40.6%	52	29	40.3%	0.3%	1.000

All Adverse Events	prodisc® L			Fusion			Dif	Exact
	Events	Subjs	%*	Events	Subjs	%*	%*	p[1]
genitourinary	28	25	15.2%	12	10	13.9%	1.3%	1.000
headache	22	18	10.9%	12	10	13.9%	-3.0%	0.517
hernia	1	1	0.6%	0	0	0.0%	0.6%	1.000
incontinence	5	5	3.0%	1	1	1.4%	1.6%	0.670
insomnia	23	22	13.3%	12	10	13.9%	-0.6%	1.000
migration not requiring surgery	1	1	0.6%	0	0	0.0%	0.6%	1.000
narcotics use	8	8	4.8%	0	0	0.0%	4.8%	0.110
neoplasm	1	1	0.6%	1	1	1.4%	-0.8%	0.516
other	38	28	17.0%	19	13	18.1%	-1.1%	0.853
other musculoskeletal	24	20	12.1%	11	11	15.3%	-3.2%	0.533
pain other (not back/hip/leg)	40	34	20.6%	25	17	23.6%	-3.0%	0.610
pseudoarthrosis	0	0	0.0%	4	4	5.6%	-5.6%	0.008
psychological	41	32	19.4%	17	12	16.7%	2.7%	0.718
respiratory	25	24	14.5%	8	8	11.1%	3.4%	0.541
spinal stenosis	1	1	0.6%	1	1	1.4%	-0.8%	0.516
subsidence not requiring surgery	9	8	4.8%	1	1	1.4%	3.5%	0.283
surgery - adjacent level	3	3	1.8%	4	4	5.6%	-3.7%	0.204
surgery - other	73	47	28.5%	21	16	22.2%	6.3%	0.342
thrombosis (dvt leg)	3	2	1.2%	2	2	2.8%	-1.6%	0.587
vertebral fracture	1	1	0.6%	1	1	1.4%	-0.8%	0.516

*Percentage of subjects experiencing specific event without regard to length of follow-up.
[1]Two-sided Fisher's Exact test.

Table 16 depicts a time course of all adverse events by category. In some cases, the available information did not allow for determination of the AE start date and therefore the time course for these events was unknown; these events are included in the Missing column.

Table 16: Counts of Specific Adverse Events by Time of Occurrence

All Adverse Events - Timecourse	Missing		0-2 days		2-42 days		42-210 days		210-730 days		730-1095 days		1095-1460 days		>1460 days		Total	
	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C
ALL	**4**	**7**	**301**	**142**	**136**	**85**	**190**	**76**	**231**	**121**	**72**	**39**	**59**	**33**	**63**	**33**	**1056**	**536**
PAIN - BACK AND LOWER EXTREMITY	**0**	**3**	**26**	**10**	**32**	**17**	**74**	**39**	**92**	**43**	**21**	**12**	**19**	**14**	**24**	**10**	**288**	**148**
pain - back	0	2	6	5	5	0	25	15	42	16	6	6	7	7	6	4	97	55
pain - back and lower extremities	0	0	5	1	7	3	16	6	20	10	4	1	7	4	4	2	63	27
pain - back and lower extremities with burning	0	0	0	0	0	0	2	1	0	1	0	0	1	0	0	0	3	2
pain - back and lower extremities with numbness at index level	0	0	0	0	1	0	3	1	2	1	2	1	0	0	1	0	9	3
pain - back and other	0	0	10	4	0	0	0	0	4	0	0	1	0	0	1	0	15	5
pain - groin area	0	0	2	0	3	1	1	0	1	0	0	1	0	0	0	1	7	3
pain - lower extremities	0	1	2	0	15	9	26	13	20	13	8	2	2	2	10	3	83	43
pain - lower extremities and incision site	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	1	1
pain - lower extremities with numbness at index level	0	0	1	0	1	4	0	3	3	1	1	0	2	1	2	0	10	9

All Adverse Events - Timecourse	Missing		0-2 days		2-42 days		42-210 days		210-730 days		730-1095 days		1095-1460 days		>1460 days		Total	
	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C
NEUROLOGICAL EVENTS	**0**	**0**	**6**	**5**	**8**	**2**	**17**	**2**	**22**	**14**	**3**	**1**	**0**	**1**	**1**	**3**	**57**	**28**
motor deficit in index level	0	0	1	0	0	0	1	0	2	1	0	0	0	0	0	0	4	1
neurological	0	0	0	1	0	1	0	0	5	0	0	0	0	0	0	0	5	2
numbness index level related	0	0	0	0	0	0	2	1	2	2	1	0	0	0	0	1	5	4
numbness peripheral nerve or non-index level related	0	0	5	4	8	1	14	1	13	10	2	1	0	1	1	2	43	20
reflex change	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1
DEGENERATIVE DISEASE PROGRESSION	**0**	**0**	**0**	**0**	**0**	**0**	**1**	**1**	**5**	**5**	**2**	**1**	**3**	**0**	**4**	**2**	**15**	**9**
degenerative disease progression, non-lumbar	0	0	0	0	0	0	1	1	2	0	1	0	1	0	2	0	7	1
degenerative disease progression, other lumbar	0	0	0	0	0	0	0	0	2	5	1	1	2	0	2	2	7	8
herniated nucleus pulposus	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0
ADDITIONAL SURGERY INDEX LEVEL	**0**	**0**	**0**	**0**	**2**	**0**	**1**	**0**	**1**	**7**	**0**	**3**	**0**	**2**	**1**	**2**	**5**	**14**
migration requiring surgery	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0
surgery - index level (other)	0	0	0	0	1	0	1	0	1	0	0	0	0	0	0	0	3	0
surgery - index level (revision)	0	0	0	0	0	0	0	0	0	7	0	3	0	2	0	2	0	14
surgery - index level (supplemental fixation)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0
INCISION SITE RELATED	**0**	**0**	**15**	**6**	**16**	**12**	**8**	**2**	**2**	**3**	**1**	**0**	**0**	**0**	**0**	**0**	**42**	**23**
infection - superficial wound with incision site pain	0	0	2	0	2	5	2	0	0	1	0	0	0	0	0	0	6	6
pain - incision site	0	0	9	3	4	2	5	2	1	2	0	0	0	0	0	0	19	9
wound issues, other	0	0	4	3	10	5	1	0	1	0	1	0	0	0	0	0	17	8
INFECTION, NOT INDEX LEVEL RELATED	**0**	**0**	**6**	**0**	**2**	**1**	**4**	**2**	**3**	**3**	**3**	**1**	**2**	**0**	**0**	**0**	**20**	**7**
infection - other non-wound related	0	0	4	0	0	0	3	0	3	3	3	1	1	0	0	0	14	4
infection - uti	0	0	1	0	2	1	0	1	0	0	0	0	1	0	0	0	4	2
pulmonary infection	0	0	1	0	0	0	1	1	0	0	0	0	0	0	0	0	2	1
MUSCULOSKELETAL SPASMS	**0**	**0**	**20**	**3**	**8**	**4**	**11**	**4**	**8**	**2**	**0**	**1**	**0**	**0**	**2**	**1**	**49**	**15**
musculoskeletal spasms - back	0	0	10	2	2	2	5	3	6	1	0	0	0	0	1	1	24	9
musculoskeletal spasms - back and leg	0	0	0	0	1	0	1	0	2	0	0	1	0	0	1	0	5	1
musculoskeletal spasms - leg	0	0	1	0	4	1	5	1	0	1	0	0	0	0	0	0	10	3
non-specific musculoskeletal spasms	0	0	9	1	1	1	0	0	0	0	0	0	0	0	0	0	10	2
DERMATOLOGICAL OR DRUG ALLERGY	**0**	**0**	**8**	**5**	**3**	**3**	**4**	**3**	**4**	**5**	**0**	**0**	**1**	**0**	**0**	**0**	**20**	**16**
dermatological	0	0	0	1	2	1	2	3	3	3	0	0	1	0	0	0	8	8
drug allergy/reaction	0	0	0	1	1	0	1	0	0	2	0	0	0	0	0	0	2	3
pruritus	0	0	8	3	0	2	1	0	1	0	0	0	0	0	0	0	10	5
VASCULAR INJURY	**0**	**0**	**10**	**6**	**0**	**1**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**10**	**7**
clinically significant blood loss (>1500 cc)	0	0	6	5	0	1	0	0	0	0	0	0	0	0	0	0	6	6
vessel damage/bleeding, major	0	0	2	1	0	0	0	0	0	0	0	0	0	0	0	0	2	1
vessel damage/bleeding, minor	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0
OTHER	**4**	**4**	**210**	**107**	**65**	**45**	**70**	**23**	**94**	**39**	**42**	**20**	**34**	**16**	**31**	**15**	**550**	**269**
anemia	0	0	10	13	1	2	0	0	0	0	0	0	0	0	0	0	11	15
bowel perforation	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
burning or dysesthetic pain	0	0	1	0	4	0	2	3	3	0	0	0	0	0	0	0	10	3
cardiovascular	0	0	11	6	2	1	0	0	2	0	0	4	4	0	1	0	20	11

All Adverse Events - Timecourse	Missing		0-2 days		2-42 days		42-210 days		210-730 days		730-1095 days		1095-1460 days		>1460 days		Total	
	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C	I	C
death	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	1	2	1
dizziness	0	0	4	2	1	1	1	1	1	0	0	0	0	0	0	0	7	4
dural tear	0	0	1	3	0	0	0	0	0	0	0	0	0	0	0	0	1	3
edema	0	0	2	3	5	3	4	2	2	0	2	0	0	0	0	0	15	8
fatigue	0	0	1	2	0	0	0	0	0	0	0	0	0	0	0	0	1	2
fever	0	0	30	14	2	1	0	0	0	0	0	0	0	0	0	0	32	15
fracture (non-vertebral)	0	0	0	0	0	0	0	2	1	1	2	0	0	0	3	0	6	3
gastrointestinal	0	0	60	29	19	17	8	1	6	2	3	0	1	3	1	0	98	52
genitourinary	0	0	9	3	5	3	7	0	3	3	1	0	2	2	1	1	28	12
headache	0	0	11	7	1	2	2	0	7	2	0	1	0	0	1	0	22	12
hernia	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0
incontinence	1	0	0	0	2	0	2	0	0	1	0	0	0	0	0	0	5	1
insomnia	0	0	15	2	6	4	2	2	0	3	0	0	0	0	0	1	23	12
migration not requiring surgery	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0
narcotics use	0	0	0	0	2	0	2	0	3	0	1	0	0	0	0	0	8	0
neoplasm	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	1	1
other	0	2	19	10	2	2	2	1	6	1	2	2	4	1	3	0	38	19
other musculoskeletal	0	0	1	1	2	1	6	4	8	3	3	1	2	1	2	0	24	11
pain other (not back/hip/leg)	0	0	2	1	1	0	12	3	11	12	2	2	5	2	6	5	39	25
pseudoarthrosis	0	0	0	0	0	0	0	0	0	3	0	0	0	1	0	0	0	4
psychological	0	0	15	5	2	1	8	3	7	3	5	1	3	1	1	3	41	17
respiratory	0	0	15	6	3	0	1	1	3	1	2	0	1	0	0	0	25	8
spinal stenosis	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	1	1
subsidence not requiring surgery	3	1	0	0	3	0	3	0	0	0	0	0	0	0	0	0	9	1
surgery - adjacent level	0	0	0	0	0	0	0	0	2	0	0	2	1	1	0	1	3	4
surgery - other	0	1	0	0	1	4	7	0	24	4	18	6	11	4	12	2	73	21
thrombosis (dvt leg)	0	0	1	0	0	2	0	0	2	0	0	0	0	0	0	0	3	2
vertebral fracture	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	1	1

The adverse events categorized by severity are presented in Table 17 for the pro**disc**® L group and Table 18 for the Fusion group.

Table 17: Counts of Specific Adverse Events by Severity in the prodisc® L Group

	Mild		Moderate		Severe		Death		Total
	Events	%*	Events	%*	Events	%*	Events	%*	Events
ALL	**543**	**51.3%**	**426**	**40.3%**	**87**	**8.2%**	**2**	**0.2%**	**1058**
PAIN - BACK AND LOWER EXTREMITY	**129**	**44.8%**	**133**	**46.2%**	**26**	**9.0%**	**0**	**0.0%**	**288**
pain - back	47	48.5%	43	44.3%	7	7.2%	0	0.0%	97
pain - back and lower extremities	24	38.1%	33	52.4%	6	9.5%	0	0.0%	63
pain - back and lower extremities with burning	1	33.3%	2	66.7%	0	0.0%	0	0.0%	3
pain - back and lower extremities with numbness at index level	1	11.1%	7	77.8%	1	11.1%	0	0.0%	9
pain - back and other	1	6.7%	6	40.0%	8	53.3%	0	0.0%	15
pain - groin area	5	71.4%	2	28.6%	0	0.0%	0	0.0%	7
pain - lower extremities	45	54.2%	35	42.2%	3	3.6%	0	0.0%	83

	Mild		Moderate		Severe		Death		Total
	Events	%*	Events	%*	Events	%*	Events	%*	Events
pain - lower extremities and incision site	1	100%	0	0.0%	0	0.0%	0	0.0%	1
pain - lower extremities with numbness at index level	4	40.0%	5	50.0%	1	10.0%	0	0.0%	10
NEUROLOGICAL EVENTS	**38**	**65.5%**	**19**	**32.8%**	**1**	**1.7%**	**0**	**0.0%**	**58**
motor deficit in index level	2	40.0%	3	60.0%	0	0.0%	0	0.0%	5
neurological	2	40.0%	3	60.0%	0	0.0%	0	0.0%	5
numbness index level related	5	100%	0	0.0%	0	0.0%	0	0.0%	5
numbness peripheral nerve or non-index level related	29	67.4%	13	30.2%	1	2.3%	0	0.0%	43
reflex change	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0
DEGENERATIVE DISEASE PROGRESSION	**2**	**13.3%**	**10**	**66.7%**	**3**	**20.0%**	**0**	**0.0%**	**15**
degenerative disease progression, non-lumbar	0	0.0%	6	85.7%	1	14.3%	0	0.0%	7
degenerative disease progression, other lumbar	2	28.6%	4	57.1%	1	14.3%	0	0.0%	7
herniated nucleus pulposus	0	0.0%	0	0.0%	1	100%	0	0.0%	1
ADDITIONAL SURGERY INDEX LEVEL	**0**	**0.0%**	**1**	**20.0%**	**4**	**80.0%**	**0**	**0.0%**	**5**
migration requiring surgery	0	0.0%	0	0.0%	1	100%	0	0.0%	1
surgery - index level (other)	0	0.0%	1	33.3%	2	66.7%	0	0.0%	3
surgery - index level (revision)	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0
surgery - index level (supplemental fixation)	0	0.0%	0	0.0%	1	100%	0	0.0%	1
INCISION SITE RELATED	**32**	**76.2%**	**8**	**19.0%**	**2**	**4.8%**	**0**	**0.0%**	**42**
infection - superficial wound with incision site pain	4	66.7%	2	33.3%	0	0.0%	0	0.0%	6
pain - incision site	11	57.9%	6	31.6%	2	10.5%	0	0.0%	19
wound issues, other	17	100%	0	0.0%	0	0.0%	0	0.0%	17
INFECTION, NOT INDEX LEVEL RELATED	**13**	**65.0%**	**6**	**30.0%**	**1**	**5.0%**	**0**	**0.0%**	**20**
infection - other non-wound related	8	57.1%	5	35.7%	1	7.1%	0	0.0%	14
infection - uti	3	75.0%	1	25.0%	0	0.0%	0	0.0%	4
pulmonary infection	2	100%	0	0.0%	0	0.0%	0	0.0%	2
MUSCULOSKELETAL SPASMS	**30**	**61.2%**	**18**	**36.7%**	**1**	**2.0%**	**0**	**0.0%**	**49**
musculoskeletal spasms - back	15	62.5%	9	37.5%	0	0.0%	0	0.0%	24
musculoskeletal spasms - back and leg	3	60.0%	2	40.0%	0	0.0%	0	0.0%	5
musculoskeletal spasms - leg	7	70.0%	3	30.0%	0	0.0%	0	0.0%	10
non-specific musculoskeletal spasms	5	50.0%	4	40.0%	1	10.0%	0	0.0%	10
DERMATOLOGICAL OR DRUG ALLERGY	**17**	**85.0%**	**3**	**15.0%**	**0**	**0.0%**	**0**	**0.0%**	**20**
dermatological	6	75.0%	2	25.0%	0	0.0%	0	0.0%	8
drug allergy/reaction	2	100%	0	0.0%	0	0.0%	0	0.0%	2
pruritus	9	90.0%	1	10.0%	0	0.0%	0	0.0%	10
VASCULAR INJURY	**5**	**50.0%**	**5**	**50.0%**	**0**	**0.0%**	**0**	**0.0%**	**10**
clinically significant blood loss (>1500 cc)	2	33.3%	4	66.7%	0	0.0%	0	0.0%	6
vessel damage/bleeding, major	2	100%	0	0.0%	0	0.0%	0	0.0%	2
vessel damage/bleeding, minor	1	50.0%	1	50.0%	0	0.0%	0	0.0%	2
OTHER	**277**	**50.3%**	**223**	**40.5%**	**49**	**8.9%**	**2**	**0.4%**	**551**
anemia	6	54.5%	4	36.4%	1	9.1%	0	0.0%	11
bowel perforation	1	100%	0	0.0%	0	0.0%	0	0.0%	1
burning or dysesthetic pain	9	90.0%	1	10.0%	0	0.0%	0	0.0%	10
cardiovascular	12	60.0%	5	25.0%	3	15.0%	0	0.0%	20

	Mild		Moderate		Severe		Death		Total
	Events	%*	Events	%*	Events	%*	Events	%*	Events
death	0	0.0%	0	0.0%	0	0.0%	2	100%	2
dizziness	5	71.4%	2	28.6%	0	0.0%	0	0.0%	7
dural tear	1	100%	0	0.0%	0	0.0%	0	0.0%	1
edema	11	73.3%	4	26.7%	0	0.0%	0	0.0%	15
fatigue	0	0.0%	1	100%	0	0.0%	0	0.0%	1
fever	25	78.1%	7	21.9%	0	0.0%	0	0.0%	32
fracture (non-vertebral)	1	16.7%	4	66.7%	1	16.7%	0	0.0%	6
gastrointestinal	72	73.5%	25	25.5%	1	1.0%	0	0.0%	98
genitourinary	17	60.7%	11	39.3%	0	0.0%	0	0.0%	28
headache	7	31.8%	12	54.5%	3	13.6%	0	0.0%	22
hernia	1	100%	0	0.0%	0	0.0%	0	0.0%	1
incontinence	2	40.0%	3	60.0%	0	0.0%	0	0.0%	5
insomnia	19	82.6%	4	17.4%	0	0.0%	0	0.0%	23
migration not requiring surgery	1	100%	0	0.0%	0	0.0%	0	0.0%	1
narcotics use	3	37.5%	4	50.0%	1	12.5%	0	0.0%	8
neoplasm	0	0.0%	1	100%	0	0.0%	0	0.0%	1
other	22	57.9%	14	36.8%	2	5.3%	0	0.0%	38
other musculoskeletal	10	41.7%	14	58.3%	0	0.0%	0	0.0%	24
pain other (not back/hip/leg)	14	35.0%	25	62.5%	1	2.5%	0	0.0%	40
pseudoarthrosis	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0
psychological	15	36.6%	21	51.2%	5	12.2%	0	0.0%	41
respiratory	9	36.0%	15	60.0%	1	4.0%	0	0.0%	25
spinal stenosis	1	100%	0	0.0%	0	0.0%	0	0.0%	1
subsidence not requiring surgery	5	55.6%	4	44.4%	0	0.0%	0	0.0%	9
surgery - adjacent level	0	0.0%	1	33.3%	2	66.7%	0	0.0%	3
surgery - other	8	11.0%	38	52.1%	27	37.0%	0	0.0%	73
thrombosis (dvt leg)	0	0.0%	2	66.7%	1	33.3%	0	0.0%	3
vertebral fracture	0	0.0%	1	100%	0	0.0%	0	0.0%	1

Table 18: Counts of Specific Adverse Events by Severity in the Fusion Group

	Mild		Moderate		Severe		Death		Total
	Events	%*	Events	%*	Events	%*	Events	%*	Events
ALL	**247**	**46.0%**	**250**	**46.6%**	**37**	**6.9%**	**3**	**0.6%**	**537**
PAIN - BACK AND LOWER EXTREMITY	**57**	**38.5%**	**85**	**57.4%**	**6**	**4.1%**	**0**	**0.0%**	**148**
pain - back	17	30.9%	37	67.3%	1	1.8%	0	0.0%	55
pain - back and lower extremities	13	48.1%	14	51.9%	0	0.0%	0	0.0%	27
pain - back and lower extremities with burning	1	50.0%	1	50.0%	0	0.0%	0	0.0%	2
pain - back and lower extremities with numbness at index level	0	0.0%	3	100%	0	0.0%	0	0.0%	3
pain - back and other	0	0.0%	3	60.0%	2	40.0%	0	0.0%	5
pain - groin area	2	66.7%	1	33.3%	0	0.0%	0	0.0%	3
pain - lower extremities	20	46.5%	21	48.8%	2	4.7%	0	0.0%	43
pain - lower extremities and incision site	0	0.0%	1	100%	0	0.0%	0	0.0%	1
pain - lower extremities with numbness at index level	4	44.4%	4	44.4%	1	11.1%	0	0.0%	9
NEUROLOGICAL EVENTS	**18**	**64.3%**	**10**	**35.7%**	**0**	**0.0%**	**0**	**0.0%**	**28**
motor deficit in index level	1	100%	0	0.0%	0	0.0%	0	0.0%	1

	Mild		Moderate		Severe		Death		Total
	Events	%*	Events	%*	Events	%*	Events	%*	Events
neurological	1	50.0%	1	50.0%	0	0.0%	0	0.0%	2
numbness index level related	2	50.0%	2	50.0%	0	0.0%	0	0.0%	4
numbness peripheral nerve or non-index level related	14	70.0%	6	30.0%	0	0.0%	0	0.0%	20
reflex change	0	0.0%	1	100%	0	0.0%	0	0.0%	1
DEGENERATIVE DISEASE PROGRESSION	**4**	**44.4%**	**4**	**44.4%**	**1**	**11.1%**	**0**	**0.0%**	**9**
degenerative disease progression, non-lumbar	1	100%	0	0.0%	0	0.0%	0	0.0%	1
degenerative disease progression, other lumbar	3	37.5%	4	50.0%	1	12.5%	0	0.0%	8
herniated nucleus pulposus	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0
ADDITIONAL SURGERY INDEX LEVEL	**0**	**0.0%**	**2**	**14.3%**	**12**	**85.7%**	**0**	**0.0%**	**14**
migration requiring surgery	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0
surgery - index level (other)	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0
surgery - index level (revision)	0	0.0%	2	14.3%	12	85.7%	0	0.0%	14
surgery - index level (supplemental fixation)	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0
INCISION SITE RELATED	**11**	**47.8%**	**12**	**52.2%**	**0**	**0.0%**	**0**	**0.0%**	**23**
infection - superficial wound with incision site pain	2	33.3%	4	66.7%	0	0.0%	0	0.0%	6
pain - incision site	4	44.4%	5	55.6%	0	0.0%	0	0.0%	9
wound issues, other	5	62.5%	3	37.5%	0	0.0%	0	0.0%	8
INFECTION, NOT INDEX LEVEL RELATED	**4**	**57.1%**	**3**	**42.9%**	**0**	**0.0%**	**0**	**0.0%**	**7**
infection - other non-wound related	2	50.0%	2	50.0%	0	0.0%	0	0.0%	4
infection - uti	2	100%	0	0.0%	0	0.0%	0	0.0%	2
pulmonary infection	0	0.0%	1	100%	0	0.0%	0	0.0%	1
MUSCULOSKELETAL SPASMS	**7**	**46.7%**	**8**	**53.3%**	**0**	**0.0%**	**0**	**0.0%**	**15**
musculoskeletal spasms - back	3	33.3%	6	66.7%	0	0.0%	0	0.0%	9
musculoskeletal spasms - back and leg	1	100%	0	0.0%	0	0.0%	0	0.0%	1
musculoskeletal spasms - leg	3	100%	0	0.0%	0	0.0%	0	0.0%	3
non-specific musculoskeletal spasms	0	0.0%	2	100%	0	0.0%	0	0.0%	2
DERMATOLOGICAL OR DRUG ALLERGY	**12**	**75.0%**	**4**	**25.0%**	**0**	**0.0%**	**0**	**0.0%**	**16**
dermatological	6	75.0%	2	25.0%	0	0.0%	0	0.0%	8
drug allergy/reaction	2	66.7%	1	33.3%	0	0.0%	0	0.0%	3
pruritus	4	80.0%	1	20.0%	0	0.0%	0	0.0%	5
VASCULAR INJURY	**1**	**14.3%**	**6**	**85.7%**	**0**	**0.0%**	**0**	**0.0%**	**7**
clinically significant blood loss (>1500 cc)	1	16.7%	5	83.3%	0	0.0%	0	0.0%	6
vessel damage/bleeding, major	0	0.0%	1	100%	0	0.0%	0	0.0%	1
vessel damage/bleeding, minor	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0
OTHER	**133**	**49.3%**	**116**	**43.0%**	**18**	**6.7%**	**3**	**1.1%**	**270**
anemia	7	46.7%	8	53.3%	0	0.0%	0	0.0%	15
bowel perforation	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0
burning or dysesthetic pain	3	100%	0	0.0%	0	0.0%	0	0.0%	3
cardiovascular	0	0.0%	10	90.9%	1	9.1%	0	0.0%	11
death	0	0.0%	0	0.0%	0	0.0%	2	100%	2
dizziness	4	100%	0	0.0%	0	0.0%	0	0.0%	4
dural tear	3	100%	0	0.0%	0	0.0%	0	0.0%	3
edema	5	62.5%	3	37.5%	0	0.0%	0	0.0%	8
fatigue	1	50.0%	1	50.0%	0	0.0%	0	0.0%	2

	Mild		Moderate		Severe		Death		Total
	Events	%*	Events	%*	Events	%*	Events	%*	Events
fever	11	73.3%	3	20.0%	1	6.7%	0	0.0%	15
fracture (non-vertebral)	2	66.7%	1	33.3%	0	0.0%	0	0.0%	3
gastrointestinal	32	61.5%	18	34.6%	2	3.8%	0	0.0%	52
genitourinary	5	41.7%	6	50.0%	1	8.3%	0	0.0%	12
headache	10	83.3%	2	16.7%	0	0.0%	0	0.0%	12
hernia	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0
incontinence	0	0.0%	1	100%	0	0.0%	0	0.0%	1
insomnia	7	58.3%	5	41.7%	0	0.0%	0	0.0%	12
migration not requiring surgery	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0
narcotics use	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0
neoplasm	0	0.0%	0	0.0%	0	0.0%	1	100%	1
other	13	68.4%	5	26.3%	1	5.3%	0	0.0%	19
other musculoskeletal	5	45.5%	6	54.5%	0	0.0%	0	0.0%	11
pain other (not back/hip/leg)	11	44.0%	13	52.0%	1	4.0%	0	0.0%	25
pseudoarthrosis	1	25.0%	3	75.0%	0	0.0%	0	0.0%	4
psychological	6	35.3%	10	58.8%	1	5.9%	0	0.0%	17
respiratory	3	37.5%	5	62.5%	0	0.0%	0	0.0%	8
spinal stenosis	0	0.0%	0	0.0%	1	100%	0	0.0%	1
subsidence not requiring surgery	1	100%	0	0.0%	0	0.0%	0	0.0%	1
surgery - adjacent level	0	0.0%	0	0.0%	4	100%	0	0.0%	4
surgery - other	3	14.3%	13	61.9%	5	23.8%	0	0.0%	21
thrombosis (dvt leg)	0	0.0%	2	100%	0	0.0%	0	0.0%	2
vertebral fracture	0	0.0%	1	100%	0	0.0%	0	0.0%	1

Definitely and Probably Device-Related Adverse Events

Table 19 summarizes the adverse events that were both deemed definitely and probably related to the devices for pro**disc**® L (n=153 total adverse events) and Fusion groups (n=70 total adverse events).

Table 19: Counts and Percentages of Subjects with Definitively and Probably Device-Related Adverse Events

Implant Related (Definite and Probable) Adverse Events	prodisc® L			Fusion			Dif	Exact
	Events	Subjs	%*	Events	Subjs	%*	%*	p[1]
ALL	**2**	**2**	**1.2%**	**2**	**2**	**2.8%**	**-1.6%**	**0.587**
PAIN - BACK AND LOWER EXTREMITY	**0**	**0**	**0.0%**	**2**	**2**	**2.8%**	**-2.8%**	**0.091**
pain - back	0	0	0.0%	2	2	2.8%	-2.8%	0.091
ADDITIONAL SURGERY INDEX LEVEL	**1**	**1**	**0.6%**	**0**	**0**	**0.0%**	**0.6%**	**1.000**
migration requiring surgery	1	1	0.6%	0	0	0.0%	0.6%	1.000
OTHER	**1**	**1**	**0.6%**	**0**	**0**	**0.0%**	**0.6%**	**1.000**
subsidence not requiring surgery	1	1	0.6%	0	0	0.0%	0.6%	1.000

*Percentage of subjects experiencing specific event without regard to length of follow-up.
[1]Two-sided Fisher's Exact test.

Definitely and Probably Surgery-Related Adverse Events

Table 20 summarizes the adverse events that were both deemed definitely and probably related to the surgical procedure for the pro**disc**® L and Fusion groups. There were a total of 264 adverse events in 98 subjects in the pro**disc**® L group, and 161 adverse events in 48 subjects in the Fusion group that were considered definitely and probably related to the surgical procedure. For each AE, the CEC indicated either agreement or disagreement with the original designations that were made by the investigator (for implant relatedness, surgery relatedness, and severity) or sponsor (for severe/life-threatening status and AE category). Unanimous agreement of the CEC was required for all decisions to agree or disagree/revise a prior designation.

Table 20: Counts and Percentages of Subjects with Definitively Surgery-Related Adverse Events

Surgery Related (Definite and Probable) Adverse Events	prodisc® L n=165			Fusion n=72			Dif	Exact
	Events	Subjs	%*	Events	Subjs	%*	%*	p[1]
ALL	**264**	**98**	**59.4%**	**161**	**48**	**66.7%**	**-7.3%**	**0.312**
PAIN - BACK AND LOWER EXTREMITY	**41**	**37**	**22.4%**	**30**	**20**	**27.8%**	**-5.4%**	**0.410**
pain - back	5	5	3.0%	6	6	8.3%	-5.3%	0.094
pain - back and lower extremities	10	10	6.1%	5	5	6.9%	-0.9%	0.778
pain - back and lower extremities with numbness at index level	0	0	0.0%	1	1	1.4%	-1.4%	0.304
pain - back and other	9	9	5.5%	4	4	5.6%	-0.1%	1.000
pain - groin area	2	2	1.2%	0	0	0.0%	1.2%	1.000
pain - lower extremities	13	12	7.3%	9	7	9.7%	-2.4%	0.604
pain - lower extremities and incision site	0	0	0.0%	1	1	1.4%	-1.4%	0.304
pain - lower extremities with numbness at index level	2	2	1.2%	4	4	5.6%	-4.3%	0.071
NEUROLOGICAL EVENTS	**10**	**10**	**6.1%**	**5**	**4**	**5.6%**	**0.5%**	**1.000**
motor deficit in index level	1	1	0.6%	0	0	0.0%	0.6%	1.000
numbness peripheral nerve or non-index level related	9	9	5.5%	5	4	5.6%	-0.1%	1.000
DEGENERATIVE DISEASE PROGRESSION	**0**	**0**	**0.0%**	**1**	**1**	**1.4%**	**-1.4%**	**0.304**
degenerative disease progression, other lumbar	0	0	0.0%	1	1	1.4%	-1.4%	0.304
ADDITIONAL SURGERY INDEX LEVEL	**0**	**0**	**0.0%**	**4**	**4**	**5.6%**	**-5.6%**	**0.008**
surgery - index level (revision)	0	0	0.0%	4	4	5.6%	-5.6%	0.008
INCISION SITE RELATED	**34**	**29**	**17.6%**	**20**	**18**	**25.0%**	**-7.4%**	**0.216**
infection - superficial wound with incision site pain	5	5	3.0%	6	6	8.3%	-5.3%	0.094
pain - incision site	14	14	8.5%	6	6	8.3%	0.2%	1.000
wound issues, other	15	13	7.9%	8	7	9.7%	-1.8%	0.620
INFECTION, NOT INDEX LEVEL RELATED	**4**	**4**	**2.4%**	**1**	**1**	**1.4%**	**1.0%**	**1.000**
infection - other non-wound related	1	1	0.6%	0	0	0.0%	0.6%	1.000
infection – uti**	3	3	1.8%	1	1	1.4%	0.4%	1.000
MUSCULOSKELETAL SPASMS	**16**	**13**	**7.9%**	**5**	**5**	**6.9%**	**0.9%**	**1.000**
musculoskeletal spasms - back	8	8	4.8%	4	4	5.6%	-0.7%	0.758
musculoskeletal spasms - leg	3	3	1.8%	0	0	0.0%	1.8%	0.555
non-specific musculoskeletal spasms	5	3	1.8%	1	1	1.4%	0.4%	1.000
DERMATOLOGICAL OR DRUG ALLERGY	**2**	**2**	**1.2%**	**0**	**0**	**0.0%**	**1.2%**	**1.000**
drug allergy/reaction	1	1	0.6%	0	0	0.0%	0.6%	1.000
pruritus	1	1	0.6%	0	0	0.0%	0.6%	1.000
VASCULAR INJURY	**10**	**10**	**6.1%**	**7**	**7**	**9.7%**	**-3.7%**	**0.411**
clinically significant blood loss (>1500 cc)	6	6	3.6%	6	6	8.3%	-4.7%	0.194

Surgery Related (Definite and Probable) Adverse Events	prodisc® L n=165			Fusion n=72			Dif	Exact
	Events	Subjs	%*	Events	Subjs	%*	%*	p[1]
vessel damage/bleeding, major	2	2	1.2%	1	1	1.4%	-0.2%	1.000
vessel damage/bleeding, minor	2	2	1.2%	0	0	0.0%	1.2%	1.000
OTHER	**147**	**75**	**45.5%**	**88**	**36**	**50.0%**	**-4.5%**	**0.572**
anemia	11	11	6.7%	14	11	15.3%	-8.6%	0.050
bowel perforation	1	1	0.6%	0	0	0.0%	0.6%	1.000
burning or dysesthetic pain	1	1	0.6%	0	0	0.0%	0.6%	1.000
cardiovascular	8	7	4.2%	5	3	4.2%	0.1%	1.000
dizziness	1	1	0.6%	0	0	0.0%	0.6%	1.000
dural tear	1	1	0.6%	3	3	4.2%	-3.6%	0.085
edema	3	3	1.8%	3	3	4.2%	-2.3%	0.372
fatigue	0	0	0.0%	1	1	1.4%	-1.4%	0.304
fever	22	22	13.3%	12	10	13.9%	-0.6%	1.000
gastrointestinal	54	42	25.5%	30	21	29.2%	-3.7%	0.632
genitourinary	6	6	3.6%	3	3	4.2%	-0.5%	1.000
headache	1	1	0.6%	0	0	0.0%	0.6%	1.000
migration not requiring surgery	1	1	0.6%	0	0	0.0%	0.6%	1.000
other	8	8	4.8%	3	3	4.2%	0.7%	1.000
other musculoskeletal	2	2	1.2%	1	1	1.4%	-0.2%	1.000
pseudoarthrosis	0	0	0.0%	1	1	1.4%	-1.4%	0.304
respiratory	10	10	6.1%	5	5	6.9%	-0.9%	0.778
subsidence not requiring surgery	9	8	4.8%	0	0	0.0%	4.8%	0.110
surgery - adjacent level	0	0	0.0%	1	1	1.4%	-1.4%	0.304
surgery - other	6	4	2.4%	4	3	4.2%	-1.7%	0.437
thrombosis (dvt leg)[+]	1	1	0.6%	2	2	2.8%	-2.2%	0.220
vertebral fracture	1	1	0.6%	0	0	0.0%	0.6%	1.000

*Percentage of subjects experiencing specific event without regard to length of follow-up.
**Urinary tract infection
[+]Deep vein thrombosis
[1]Two-sided Fisher's Exact test.

All Severe or Life-Threatening Adverse Events

All adverse events that were categorized as severe or life-threatening are presented in Table 21. Compared to the Fusion subjects, the pro**disc**® L subjects exhibited a lower overall rate of any severe or life-threatening adverse events (24.8 vs. 36.1%).

Table 21: Counts and Percentages of Subjects with Severe or Life-Threatening Adverse Events

Severe and Life-threatening Adverse Events	prodisc® L (n=165)			Fusion (n=72)			Dif	Exact
	Events	Subjs	%*	Events	Subjs	%*	%*	p[1]
ALL	**65**	**41**	**24.8%**	**42**	**26**	**36.1%**	**-11.3%**	**0.086**
NEUROLOGICAL EVENTS	**1**	**1**	**0.6%**	**0**	**0**	**0.0%**	**0.6%**	**1.000**
numbness peripheral nerve or non-index level related	1	1	0.6%	0	0	0.0%	0.6%	1.000
ADDITIONAL SURGERY INDEX LEVEL	**3**	**3**	**1.8%**	**6**	**5**	**6.9%**	**-5.1%**	**0.058**
migration requiring surgery	1	1	0.6%	0	0	0.0%	0.6%	1.000
surgery - index level (other)	1	1	0.6%	0	0	0.0%	0.6%	1.000
surgery - index level (revision)	0	0	0.0%	6	5	6.9%	-6.9%	0.002

Severe and Life-threatening Adverse Events	prodisc® L (n=165)			Fusion (n=72)			Dif	Exact
	Events	Subjs	%*	Events	Subjs	%*	%*	p[1]
surgery - index level (supplemental fixation)	1	1	0.6%	0	0	0.0%	0.6%	1.000
INCISION SITE RELATED	**0**	**0**	**0.0%**	**5**	**5**	**6.9%**	**-6.9%**	**0.002**
infection - superficial wound with incision site pain	0	0	0.0%	4	4	5.6%	-5.6%	0.008
wound issues, other	0	0	0.0%	1	1	1.4%	-1.4%	0.304
INFECTION, NOT INDEX LEVEL RELATED	**3**	**3**	**1.8%**	**1**	**1**	**1.4%**	**0.4%**	**1.000**
infection - other non-wound related	3	3	1.8%	1	1	1.4%	0.4%	1.000
VASCULAR INJURY	**9**	**9**	**5.5%**	**6**	**6**	**8.3%**	**-2.9%**	**0.397**
clinically significant blood loss (>1500 cc)	6	6	3.6%	6	6	8.3%	-4.7%	0.194
vessel damage/bleeding, major	2	2	1.2%	0	0	0.0%	1.2%	1.000
vessel damage/bleeding, minor	1	1	0.6%	0	0	0.0%	0.6%	1.000
OTHER	**49**	**33**	**20.0%**	**24**	**16**	**22.2%**	**-2.2%**	**0.729**
anemia	1	1	0.6%	0	0	0.0%	0.6%	1.000
cardiovascular	2	2	1.2%	1	1	1.4%	-0.2%	1.000
death	2	2	1.2%	1	1	1.4%	-1.6%	0.587
gastrointestinal	1	1	0.6%	3	1	1.4%	-0.8%	0.516
genitourinary	0	0	0.0%	1	1	1.4%	-1.4%	0.304
headache	3	3	1.8%	0	0	0.0%	1.8%	0.555
narcotics use	1	1	0.6%	0	0	0.0%	0.6%	1.000
neoplasm	1	1	0.6%	1	1	1.4%	-0.8%	0.516
other	2	2	1.2%	0	0	0.0%	1.2%	1.000
pain other (not back/hip/leg)	1	1	0.6%	1	1	1.4%	-0.8%	0.516
psychological	3	2	1.2%	0	0	0.0%	1.2%	1.000
respiratory	2	2	1.2%	0	0	0.0%	1.2%	1.000
surgery - adjacent level	1	1	0.6%	2	2	2.8%	-2.2%	0.220
surgery - other	26	19	11.5%	12	10	13.9%	-2.4%	0.668
thrombosis (dvt leg)	3	2	1.2%	2	2	2.8%	-1.6%	0.587

*Percentage of subjects experiencing specific event without regard to length of follow-up.
[1]Two-sided Fisher's Exact test.

Secondary Surgical Interventions at the Treated Level

Within the Per Protocol cohort, the rate of subsequent surgical intervention (SSI) was 2.5% (4/161) for pro**disc**® L subjects and 10.3% (7/68) for the Fusion subjects through Month 24 and 3.1% (5/161) for pro**disc**® L subjects and 17.6% (12/68) for the Fusion subjects through Month 60. The five subsequent surgeries in the pro**disc**® L group included foraminotomies, subsequent decompression, facetectomies, and, in a single subject, removal of one of the two implanted pro**disc**® L devices due to device migration. The primary reason for the pro**disc**® L SSIs was increased pain at the treated level. In contrast, the SSIs for the Fusion group were primarily related to pain, pseudarthrosis, or disease progression.

Time-course details of the SSIs are presented in Table 22 and procedure details are provided in Table 23.

Table 22: Time course of all secondary surgical procedures at the index level – Randomized

	Wk. 6		Mo 3		Mo 6		Mo 12		Mo 18		Mo 24		Mo 36		Mo 48		Mo 60		Total	
	F	**P**	**F**	**P**	**F**	**P**	**F**	**P**	**F**	**P**	**F**	**P**	**F**	**P**	**F**	**P**	**F**	**P**	**F**	**P**
Reoperation	0	1	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	3
Removal	0	0	0	1	0	0	0	0	3	0	4	0	3	0	0	0	2	0	12	1
Revision	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	1	2	1
Supp. Fix	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL	0	1	0	1	0	0	0	0	3	1	4	1	4	0	1	0	2	1	14	5

Table 23: Secondary Surgical Intervention at the Index Level – Procedure Details

Associated AE Description	Secondary Surgical Intervention Details	Time Post-op
prodisc® L		
Subject twisted and felt pain shoot down left lower extremities	Reoperation: foraminotomy L5-S1	1 Month
Anterior migration of the superior L4-5 pro**disc**® L component	Removal of pro**disc**® L with subsequent anterior/posterior fusion at L4-5	1 Month
Back pain secondary to foraminal stenosis	Reoperation: laminotomies and medial facetectomies, foraminotomies at right L4-5, L5-S1 levels, right L4-5 facet joint cyst excision	13 Months
Increasing pain and numbness in right L5 nerve distribution	Reoperation: right L5-S1 facetectomy	18 Months
Right lower extremity pain	Revision: lumbar decompression of right L5 nerve root through an L4-5 laminoforaminotomy followed by semi-rigid stabilization	59 Months
Fusion		
Catching pain from fusion cage	Removal of hardware	16 Months
Back pain	Removal of hardware; caudal injections	17 Months
Pseudoarthrosis, coronal defect, definite motion, loose Ss1 screws	Removal of hardware with facetectomies, hemilaminectomies	18 Months
Continued back + left leg pain	Removal of hardware	19 Months
Gross symptomatic signs and symptoms on the right-sided buttock with radiating pain	Removal of bilateral pedicle screws at L4, L5, S1; removal of extensive scar tissue L4-S1; exploration of fusion mass L4-S1	23 Months
Back pain	Removal: hardware removal	24 Months

Leg pain and numbness	Removal of hardware	24 Months
Back and leg pain	Removal of segmental spinal instrumentation at index levels (L4-S1) with laminectomies at L2, L3, L4	30 Months
Pseudoarthrosis at L4-S1	Removal/revision posterior fusion with instrumentation at L4-S1 and iliac crest bone graft	35 Months
Leg pain and numbness	Removal of hardware; revision decompression	35 Months
Back pain	Removal of hardware	36 Months
Pseudoarthrosis L5-S1	Revision: exploration posterior fusion, removal of hardware L4-S1, replacement of hardware L5-S1, right iliac crest bone graft	38 Months
Post laminectomy syndrome	Removal/revision surgery at L5-S1	58 Months
Low back pain from hardware catching	Removal of hardware	64 Months

*Two fusion subjects required more than one surgical intervention at the treated level.

Radiographic Changes Involving Adjacent Levels and Symptoms

Adjacent level radiographic changes up to 60 months were documented and are reported in Table 24. Adjacent level radiographic degenerative changes were graded using a combination of disc space narrowing, presence of spondylolisthesis, endplate sclerosis, and osteophytes. Changes in degeneration were determined by grading the following at pre-operative and Month 60, computing the difference for each category:

a. disc height loss – graded 0 to 3
b. endplate sclerosis – graded 0 to 3
c. osteophytes – graded 0 to 3
d. spondylolisthesis – graded 1 if > 5 mm and < 10 mm, 2 if > 10 mm

Per Table 24, there was no significant difference in the number of adjacent levels that exhibited radiographic evidence of adjacent level degenerative changes defined by loss of disc height at Month 60 in the Fusion versus pro**disc**® L treatment groups (p=0.68). Change in ODI, change in SF-36 and VAS satisfaction were not significantly correlated with presence or absence of radiographic adjacent level changes in either treatment group.

Table 24: Radiographic degenerative changes at adjacent levels at Month 60: Fusion and prodisc® L

	prodisc® L (n = 134 adj. levels)	**Fusion (n = 56 adj. levels)**	**p-value***
	122 subjects	49 subjects	
0 - No Change	121/134 (90.3%)	49/56 (87.5%)	0.68
1 - 1-grade Increase	8/134 (6.0%)	5/56 (8.9%)	
2 - 2-grade Increase	2/134 (1.5%)	0/56 (0.0%)	
3 - 3-grade Increase	3/134 (2.2%)	2/56 (3.6%)	

Note: Numbers represent the number of levels.
*Two-sided Fisher's exact test comparing Fusion and pro**disc**® L

Neurological Status

A subject was considered a neurological success only if their neurological status was maintained or improved for each of four areas: motor status, sensory deficit, reflexes and straight leg raise (SLR) test. A time course of overall neurologic success for all subjects with available data from the per protocol cohort, excluding subjects with SSIs (no re-operations at the index level), is presented in Table 25.

Table 25: Overall Neurological Success – Per Protocol Cohort

	prodisc L			Fusion			Significance			
	N	n	%	N	n	%	Dif.*	95% CI †	Chi-sq ‡	Exact §
Week 06	153	126	82.4%	63	52	82.5%	-0.2%	(-11.3%, 11.0%)	0.974	0.999
Month 03	155	126	81.3%	65	53	81.5%	-0.2%	(-11.5%, 11.0%)	0.966	0.999
Month 06	148	129	87.2%	63	46	73.0%	14.1%	(1.9%, 26.4%)	0.012	0.016
Month 12	136	117	86.0%	59	46	78.0%	8.1%	(-4.0%, 20.1%)	0.163	0.206
Month 18	138	118	85.5%	49	37	75.5%	10.0%	(-3.4%, 23.4%)	0.110	0.125
Month 24	142	127	89.4%	61	46	75.4%	14.0%	(2.1%, 26.0%)	0.010	0.016
Month 36	102	92	90.2%	42	32	76.2%	14.0%	(-0.1%, 28.1%)	0.027	0.035
Month 48	93	77	82.8%	31	23	74.2%	8.6%	(-8.6%, 25.8%)	0.294	0.303
Month 60	125	110	88.0%	53	43	81.1%	6.9%	(-5.1%, 18.8%)	0.228	0.244

Notes:
* Difference in proportions (calculated as I minus C);
† 2-sided 95% CI (asymptotic);
‡ Chi-square p-value; § Fisher's exact test p-value.

2. Effectiveness Results

Due to the lack of validated clinical values for “ideal” ROM in the lumbar spine, the correlation between ROM and clinical success remains difficult. As a result, FDA requested analyses for overall success by including and excluding the ROM component. The results from these FDA-requested endpoints (with and without ROM) are presented below.

Month 24 overall success analysis for the Per Protocol population is presented in Table 26. A subject’s treatment was considered successful if and only if all components of success were met at that time point. Conversely, if one or more components of success was a failure, even if that subject had incomplete data, that subject was treated as a failure. For the radiographic endpoint criteria, each level was assessed separately and both levels needed to meet the success criterion for the subject to be considered a success for that criterion. Given the high rates of success in the radiographic components and occasional issues with analyzing radiographs due to image quality (demonstrated by the lower rate of ROM and disc height follow-up compared to the clinical follow-up), subjects with missing radiographic data but considered a success for other components of the endpoint were considered as overall successes.

Table 26: Overall Success including and excluding the radiographic data at Month 24 – Per Protocol Cohort

	prodisc L			Fusion			95% CILB
	N	n	%	N	n	%	One-sided
No secondary surgical interventions	**161**	**157**	**97.5%**	**68**	**61**	**89.7%**	**-4.1%**
No revisions	161	161	100.0%	68	68	100.0%	.
No removals	161	160	99.4%	68	61	89.7%	-2.3%
No supplemental fixations	161	161	100.0%	68	68	100.0%	.
No reoperations	161	158	98.1%	68	68	100.0%	-13.7%
No new neurological deficit	**142**	**127**	**89.4%**	**61**	**46**	**75.4%**	**1.5%**
ODI improvement of at least 15 points	**143**	**104**	**72.7%**	**61**	**35**	**57.4%**	**2.7%**
SF36 PCS improvement (>0)	**142**	**123**	**86.6%**	**58**	**46**	**79.3%**	**-5.5%**
Radiographic success	**129**	**110**	**85.3%**	**57**	**43**	**75.4%**	**-3.3%**
Range of motion success	131	117	89.3%	60	60	100.0%	-23.3%
Bridging bone success	141	141	100.0%	60	49	81.7%	5.6%
Disc height success	135	135	100.0%	57	54	94.7%	-7.7%
Migration success	141	141	100.0%	60	60	100.0%	.
Radiolucency success	141	141	100.0%	60	58	96.7%	-9.3%
Subsidence success	141	136	96.5%	60	59	98.3%	-14.5%
FDA-Requested Overall Success	**143**	**80**	**55.9%**	**60**	**28**	**46.7%**	**-3.4%**
FDA-Requested Overall Success w/o ROM	**143**	**90**	**62.9%**	**60**	**28**	**46.7%**	**3.6%**

As seen in the table above, FDA requested overall success (including and excluding ROM) at 24 months for pro**disc**® L was 55.9% compared to 46.7% for Fusion, with a difference between groups of 9.2%. The lower-bound of the 1-sided 95% confidence interval for the group difference was -3.4%. Since -3.4% is greater than -10% (the FDA requested non-inferiority margin), the results from this comparison demonstrate that the success criterion for non-inferiority had been achieved. Note that subjects with missing outcomes were removed from the analysis.

After removing the ROM component of the primary endpoint, FDA requested overall success at 24 months for pro**disc**® L was 62.9% compared to 46.7% for Fusion, with a difference between groups of 16.2%. The lower-bound of the 1-sided 95% confidence interval for the group difference was 3.6%. Since 3.6% is greater than -10% (the FDA requested non-inferiority margin), the results from this comparison demonstrate that the success criterion for non-inferiority had been achieved.

For the various criteria included in the overall success assessment, pro**disc**® L was numerically greater in overall success than Fusion for all the main components of overall success (lack of secondary surgical interventions, lack of new neurological deficit, ODI improvement, SF-36 PCS improvement, radiographic success), with large differences between the groups considering the lack of new neurological deficit (pro**disc**® L: 89.4%; Fusion: 75.4%) and ≥15 point decrease in ODI (pro**disc**® L: 72.7%; Fusion: 57.4%). Within the radiographic success component, the main drivers of the overall radiographic success were ROM for pro**disc**® L and bridging bone for Fusion control group, parameters that were necessarily defined differently for the two cohorts given the comparison of a non-fusion technology to a fusion technology.

The FDA requested calculation of overall success endpoint at time points from 3 to 60 months (with and without the ROM component) for the ITT and per protocol cohorts with multiple imputation to account for subjects with missing data. Results from this assessment are presented in Table 27. The overall results from the ITT cohort were similar to the results in the per protocol cohort.

Table 27: Overall Success Measurements at Month 24 Using Multiple Imputation for Missing Data

Outcome	Pop.	Month	prodisc® L		Fusion		Diff.	95% CI LB One-sided[2]
			N	%	N	%		
FDA-Requested Overall Success	ITT (N= 255)	3	173	42.3%	82	42.2%	0.1%	-11.9%
		6		53.6%		38.7%	15.0%	3.3%
		12		51.6%		36.3%	15.3%	4.1%
		18		52.9%		37.4%	15.5%	2.3%
		24		**55.3%**		**46.7%**	**8.6%**	**-3.5%**
		36		53.4%		42.0%	11.4%	-0.4%
		48		53.5%		40.6%	12.9%	-1.1%
		60		54.0%		51.1%	2.9%	-9.1%
	PP (N= 229)	3	161	42.4%	68	42.2%	0.2%	-11.9%
		6		53.1%		39.9%	13.3%	0.6%
		12		51.4%		38.1%	13.3%	1.5%
		18		53.5%		39.4%	14.1%	0.7%
		24		**55.0%**		**47.6%**	**7.3%**	**-5.0%**
		36		54.7%		45.6%	9.1%	-6.1%
		48		56.9%		40.0%	16.9%	1.9%
		60		54.1%		50.3%	3.8%	-8.7%
FDA-Requested Overall Success w/o ROM	ITT (N= 255)	3	173	50.5%	82	44.1%	6.3%	-5.7%
		6		59.8%		39.3%	20.5%	7.8%
		12		57.8%		36.5%	21.3%	9.3%
		18		59.4%		39.6%	19.7%	7.9%
		24		**62.8%**		**47.8%**	**15.0%**	**3.1%**
		36		65.4%		42.2%	23.2%	10.4%
		48		60.6%		40.9%	19.8%	2.2%
		60		62.0%		51.0%	11.0%	-1.3%
	PP (N= 229)	3	161	51.7%	68	42.8%	8.9%	-3.3%
		6		59.3%		40.7%	18.5%	6.4%
		12		58.2%		38.8%	19.4%	7.0%
		18		59.9%		41.3%	18.6%	6.2%
		24		**62.4%**		**47.9%**	**14.5%**	**1.8%**
		36		65.5%		46.8%	18.8%	6.2%
		48		61.2%		41.2%	20.0%	6.4%
		60		62.9%		51.0%	11.8%	-1.4%

[1]Imputation model (10 imputations): Fully conditional specification (FCS) with outcome predicted by treatment group, age, BMI, sex, and month 3 through month 60 outcomes;
[2]Combined using Rubin's Rules;

Secondary Effectiveness Analysis

Oswestry Disability Index (ODI)

Table 28 summarizes ODI changes through time for subjects with available data from the per protocol cohort.

Table 28: Descriptive Statistics for ODI – Per Protocol Cohort

	prodisc L						Fusion						t-test	Wilcoxon	Effect
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p-value†	p-value‡	size§
Baseline	161	65.0	11.2	64.0	40.0	98.0	68	64.8	9.5	66.0	44.0	82.0	0.855	0.977	0.03
Week 06	155	43.9	18.2	46.0	0.0	90.0	62	50.3	17.0	55.0	6.0	84.0	0.018	0.008	-0.36
Month 03	154	38.0	20.9	42.0	0.0	86.0	65	43.9	15.2	44.0	4.0	80.0	0.040	0.061	-0.32
Month 06	147	35.1	21.9	36.0	0.0	80.0	63	43.1	17.1	44.0	4.0	80.0	0.010	0.017	-0.41
Month 12	138	33.9	24.1	34.0	0.0	78.0	60	40.4	22.5	41.0	0.0	82.0	0.079	0.078	-0.28
Month 18	137	32.9	24.9	36.0	0.0	78.0	49	43.5	22.0	44.0	0.0	82.0	0.009	0.011	-0.45
Month 24	143	30.2	24.7	26.0	0.0	86.0	61	40.1	23.1	40.0	0.0	84.0	0.009	0.007	-0.41
Month 36	102	31.4	25.1	31.0	0.0	78.0	44	41.5	23.0	42.0	0.0	80.0	0.024	0.027	-0.42
Month 48	95	32.3	24.8	34.0	0.0	80.0	32	45.6	22.2	49.0	6.0	90.0	0.008	0.009	-0.57
Month 60	125	28.2	23.4	22.0	0.0	74.0	53	39.2	24.1	42.0	0.0	84.0	0.005	0.008	-0.46

Notes:
† Two-sample pooled t-test p-value;
‡ Two-sample Wilcoxon rank sum p-value;
§ Standardized effect size (calculated as group difference in means divided by pooled within group SD).

The baseline ODI scores were not statistically different between the pro**disc**® L and fusion cohorts. At almost all timepoints after surgery, the mean ODI for pro**disc**® L subjects was lower than for the fusion subjects.

The FDA-requested success criteria for ODI was defined by a decrease of 15 points. The sponsor met this primary endpoint for ODI success. The percentage of subjects achieving ODI success at every time point is depicted in Table 29.

Table 29: Percent of Subjects with ≥15 Point Decrease in ODI – Per Protocol Cohort

	prodisc L			Fusion			Significance			
	N	n	%	N	n	%	Dif.*	95% CI †	Chi-sq ‡	Exact §
Week 06	155	88	56.8%	62	31	50.0%	6.8%	(-7.9%, 21.5%)	0.365	0.370
Month 03	154	105	68.2%	65	42	64.6%	3.6%	(-10.2%, 17.3%)	0.608	0.638
Month 06	147	102	69.4%	63	39	61.9%	7.5%	(-6.6%, 21.6%)	0.290	0.337
Month 12	138	98	71.0%	60	36	60.0%	11.0%	(-3.5%, 25.5%)	0.128	0.139
Month 18	137	97	70.8%	49	27	55.1%	15.7%	(-0.2%, 31.6%)	0.045	0.053
Month 24	143	104	72.7%	61	35	57.4%	15.4%	(1.0%, 29.7%)	0.031	0.034
Month 36	102	77	75.5%	44	26	59.1%	16.4%	(-0.4%, 33.2%)	0.046	0.051
Month 48	95	68	71.6%	32	17	53.1%	18.5%	(-1.1%, 38.0%)	0.055	0.081
Month 60	125	95	76.0%	53	32	60.4%	15.6%	(0.5%, 30.8%)	0.035	0.046

Notes:
* Difference in proportions (calculated as I minus C);
† 2-sided 95% CI (asymptotic);
‡ Chi-square p-value; § Fisher's exact test p-value.

The percent of subjects with a greater than 15-point decrease in ODI was not statistically different between the pro**disc**® L and fusion cohorts until 18 months. In most of the timepoints after 18 months, a higher percentage of pro**disc**® L subjects experienced a greater than 15-point decrease in ODI.

VAS pain

Table 30 summarizes VAS pain value changes through time for subjects with available data from the per protocol cohort.

Table 30: Descriptive Statistics for Low Back and Leg Pain (via VAS) – Per Protocol Cohort

	prodisc L						Fusion						t-test	Wilcoxon	Effect
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p-value†	p-value‡	size§
Baseline	161	75.9	16.0	77.9	30.1	100.0	68	74.9	14.0	76.3	28.4	100.0	0.646	0.341	0.07
Week 06	155	41.7	25.7	40.0	0.0	93.9	62	45.2	25.0	44.4	1.0	89.4	0.363	0.396	-0.14
Month 03	154	38.4	27.7	35.1	0.0	91.7	65	42.3	23.8	41.5	0.0	96.3	0.333	0.297	-0.15
Month 06	146	37.6	27.7	32.9	0.0	100.0	63	43.4	26.2	41.1	1.6	96.9	0.154	0.132	-0.22
Month 12	138	35.6	28.8	32.3	0.0	97.0	60	40.2	28.1	33.9	1.6	96.9	0.305	0.198	-0.16
Month 18	137	35.1	29.9	32.0	0.0	96.3	49	46.1	29.7	44.4	0.5	96.5	0.027	0.017	-0.37
Month 24	142	31.9	30.4	21.0	0.0	93.5	61	39.4	29.8	37.4	0.0	94.4	0.104	0.040	-0.25
Month 36	101	32.2	29.6	20.9	0.0	94.8	43	45.5	28.4	51.5	1.5	94.9	0.014	0.009	-0.46
Month 48	92	33.4	28.7	29.1	0.0	91.0	32	48.6	25.9	55.5	0.5	99.0	0.009	0.008	-0.55
Month 60	124	28.7	28.3	19.7	0.0	99.5	53	43.2	29.8	47.1	0.0	98.0	0.002	0.004	-0.50

Notes:
† Two-sample pooled t-test p-value;
‡ Two-sample Wilcoxon rank sum p-value;
§ Standardized effect size (calculated as group difference in means divided by pooled within group SD).

The VAS pain values were not statistically different between the pro**disc**® L and fusion cohorts until 18 months. After 18 months, pro**disc**® L subjects had lower VAS pain values than fusion subjects.

The minimal clinically important difference for VAS pain change and therefore those subjects that achieve success, were those that experience a decrease of 20mm in VAS pain. The percentage of subjects achieving VAS pain success at every time point is depicted in Table 31.

Table 31: Percent of Subjects with 20mm Decrease in Low Back and Leg Pain (via VAS) – Per Protocol Cohort

	prodisc L			Fusion			Significance			
	N	n	%	N	n	%	Dif.*	95% CI †	Chi-sq ‡	Exact §
Week 06	155	103	66.5%	62	38	61.3%	5.2%	(-9.1%, 19.4%)	0.472	0.529
Month 03	154	103	66.9%	65	45	69.2%	-2.3%	(-15.8%, 11.1%)	0.735	0.755
Month 06	146	101	69.2%	63	39	61.9%	7.3%	(-6.9%, 21.4%)	0.305	0.338
Month 12	138	99	71.7%	60	43	71.7%	0.1%	(-13.6%, 13.7%)	0.992	0.999
Month 18	137	99	72.3%	49	26	53.1%	19.2%	(3.3%, 35.1%)	0.014	0.021
Month 24	142	105	73.9%	61	37	60.7%	13.3%	(-0.9%, 27.5%)	0.058	0.067
Month 36	101	73	72.3%	43	22	51.2%	21.1%	(3.8%, 38.4%)	0.014	0.021
Month 48	92	71	77.2%	32	19	59.4%	17.8%	(-1.3%, 36.9%)	0.052	0.066
Month 60	124	94	75.8%	53	38	71.7%	4.1%	(-10.2%, 18.4%)	0.565	0.576

Notes:
* Difference in proportions (calculated as I minus C);
† 2-sided 95% CI (asymptotic);
‡ Chi-square p-value; § Fisher's exact test p-value.

Between 18 and 48 months, a higher percentage of pro**disc**® L subjects experienced at least a 20mm decrease in VAS pain scores. At other time points, there was no statistical difference in reduction of VAS pain scores between the cohorts.

VAS satisfaction

Each subject was asked to indicate their level of satisfaction with the surgery they received on a Visual Analog Scale (VAS) by directly marking on a 100 mm line printed on the CRF. The resulting VAS satisfaction score was a ratio of the subject response to the total length of the scale. Summary statistics for the VAS satisfaction are presented for subjects with available data from the per protocol cohort in Table 32.

Table 32: Descriptive Statistics for Subject Satisfaction (via VAS)

	prodisc L						Fusion						t-test	Wilcoxon	Effect
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p-value†	p-value‡	size§
Week 06	154	78.9	21.8	82.7	2.1	100.0	61	72.3	24.7	80.0	5.4	100.0	0.055	0.063	0.28
Month 03	152	78.4	23.5	88.7	0.0	100.0	65	70.5	26.1	81.1	8.5	99.0	0.029	0.006	0.32
Month 06	147	77.9	23.0	87.1	6.6	100.0	63	67.6	25.3	72.9	16.0	98.9	0.004	0.001	0.43
Month 12	137	76.6	26.7	85.9	0.0	101.0	60	67.3	31.4	78.6	2.1	100.0	0.034	0.018	0.32
Month 18	137	76.0	27.6	85.9	0.0	100.0	49	63.8	31.7	72.7	5.0	100.0	0.012	0.017	0.41
Month 24	141	78.3	27.5	90.0	0.0	100.0	61	66.2	29.8	75.0	4.2	100.0	0.006	<.001	0.42
Month 36	101	78.9	25.4	88.8	0.0	100.0	43	67.9	26.9	75.1	5.6	99.0	0.021	0.003	0.42
Month 48	94	78.2	27.4	92.6	3.0	100.0	31	69.2	28.0	72.3	9.4	100.0	0.117	0.028	0.33
Month 60	125	79.3	28.0	95.1	0.0	100.0	53	69.2	28.6	75.2	5.9	100.0	0.030	0.005	0.36

Notes:
† Two-sample pooled t-test p-value;
‡ Two-sample Wilcoxon rank sum p-value;
§ Standardized effect size (calculated as group difference in means divided by pooled within group SD).

At almost all timepoints, subject satisfaction was higher for the pro**disc**® L cohort than the fusion cohort.

Would you have the surgery again?

Subjects were asked at each time point whether they would have the same surgery again. The results for all subjects with available data from the per protocol cohort are summarized in Table 33.

Table 33: Surgery Again

		prodisc® L	Fusion	p-value*
Week 6	No. Evaluated	155	63	0.0005
	No	6 (3.9%)	5 (7.9%)	
	Maybe	18 (11.6%)	20 (31.7%)	
	Yes	131 (84.5%)	38 (60.3%)	
Month 3	No. Evaluated	150	66	0.0525
	No	6 (4.0%)	6 (9.1%)	
	Maybe	20 (13.3%)	15 (22.7%)	
	Yes	124 (82.7%)	45 (68.2%)	
Month 6	No. Evaluated	145	63	0.0035
	No	4 (2.8%)	6 (9.5%)	
	Maybe	19 (13.1%)	17 (27.0%)	
	Yes	122 (84.1%)	40 (63.5%)	
Month 12	No. Evaluated	136	59	0.0182
	No	2 (1.5%)	6 (10.2%)	
	Maybe	24 (17.6%)	12 (20.3%)	
	Yes	110 (80.9%)	41 (69.5%)	
Month 18	No. Evaluated	133	48	0.0464
	No	7 (5.3%)	7 (14.6%)	
	Maybe	18 (13.5%)	10 (20.8%)	
	Yes	108 (81.2%)	31 (64.6%)	
Month 24	No. Evaluated	139	56	0.1246
	No	11 (7.9%)	6 (10.7%)	
	Maybe	18 (12.9%)	13 (23.2%)	
	Yes	110 (79.1%)	37 (66.1%)	
Month 36	No. Evaluated	98	38	0.0548
	No	3 (3.1%)	4 (10.5%)	
	Maybe	11 (11.2%)	8 (21.1%)	
	Yes	84 (85.7%)	26 (68.4%)	
Month 48	No. Evaluated	91	26	0.3285
	No	5 (5.5%)	3 (11.5%)	
	Maybe	11 (12.1%)	1 (3.8%)	
	Yes	75 (82.4%)	22 (84.6%)	
Month 60	No. Evaluated	122	49	0.0301
	No	7 (5.7%)	6 (12.2%)	
	Maybe	11 (9.0%)	10 (20.4%)	
	Yes	104 (85.2%)	33 (67.3%)	

* Fisher's exact test comparing the distribution of responses between Fusion and pro**disc**® L

At most timepoints, the percentage of pro**disc**® L subjects who would not have the surgery again was lower and who would have the surgery again were higher than the fusion subjects.

Medication Use

Table 34 presents the usage of narcotic medication used in each treatment group. Data presented represents narcotic medication used over the eight hours preceding each protocol visit. The relationship between the use of narcotic medication and the subject's spinal pain was not captured.

Table 34: Time course of narcotic medication use: Fusion, prodisc® L

Visit	prodisc® L	Fusion	p-value*
Pre-operative	111/161 (68.9%)	42/ 68 (61.8%)	0.3568
Week 6	109/154 (70.8%)	50/ 64 (78.1%)	0.3167
Month 3	85/154 (55.2%)	50/ 66 (75.8%)	0.0042
Month 6	71/147 (48.3%)	40/ 65 (61.5%)	0.1006
Month 12	57/136 (41.9%)	33/ 62 (53.2%)	0.1664
Month 18	51/138 (37.0%)	29/ 50 (58.0%)	0.0123
Month 24	50/141 (35.5%)	33/ 57 (57.9%)	0.0044
Month 36	41/102 (40.2%)	19/ 40 (47.5%)	0.4547
Month 48	34/ 92 (37.0%)	17/ 26 (65.4%)	0.0134
Month 60	43/124 (34.7%)	29/ 49 (59.2%)	0.0038

*Two-sided Fisher's exact test comparing Fusion and pro**disc**® L

Radiographic Assessments

As pro**disc**® L devices were implanted at contiguous levels, the radiographic data below are stratified according to whether the device was implanted at the cranial (superior device) or caudal (inferior device) levels. Fusion group treated levels are described similarly.

Range of Motion

ROM was measured in flexion-extension and lateral bending for treated levels and adjacent levels. The flexion-extension ROM measurements at the index levels were utilized for the portion of the protocol-defined overall success determination, while other measurements are presented as additional information.

Flexion/extension ROM data (in degrees) over time for cranially implanted devices are summarized in Table 35, while ROM for the caudally implanted devices are summarized in Table 36.

Table 35: Descriptive Statistics for ROM (Flexion to Extension) (degrees) – Cranial Level (degrees) – Per Protocol Cohort

	prodisc L						Fusion						t-test	Wilcoxon	Effect
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p-value†	p-value‡	size§
Baseline	156	6.2	4.7	5.0	0.0	18.0	64	7.4	5.0	7.0	1.0	22.0	0.091	0.097	-0.25
Week 06	147	4.3	3.6	4.0	0.0	15.0	14	0.6	0.6	0.5	0.0	2.0	<.001	<.001	1.46
Month 03	147	5.1	3.9	4.0	0.0	18.0	27	0.5	0.7	0.0	0.0	3.0	<.001	<.001	1.63
Month 06	141	6.0	4.9	6.0	0.0	22.0	57	0.8	0.9	1.0	0.0	5.0	<.001	<.001	1.49
Month 12	132	6.4	5.1	6.0	0.0	17.0	58	0.8	1.0	1.0	0.0	5.0	<.001	<.001	1.50
Month 18	131	6.7	5.3	6.0	0.0	20.0	45	0.8	0.9	1.0	0.0	4.0	<.001	<.001	1.57
Month 24	140	7.5	5.4	8.0	0.0	24.0	60	0.8	1.1	0.5	0.0	6.0	<.001	<.001	1.73
Month 36	99	6.3	5.2	6.0	0.0	18.0	39	0.8	1.0	1.0	0.0	5.0	<.001	<.001	1.48
Month 48	83	6.3	5.0	6.0	0.0	19.0	29	1.0	1.8	0.0	0.0	8.0	<.001	<.001	1.41
Month 60	118	6.6	4.7	6.0	0.0	18.0	51	0.7	1.4	0.0	0.0	6.0	<.001	<.001	1.69

Notes:
† Two-sample pooled t-test p-value;
‡ Two-sample Wilcoxon rank sum p-value;
§ Standardized effect size (calculated as group difference in means divided by pooled within group SD).

Table 36: Descriptive Statistics for ROM (Flexion to Extension) (degrees) – Caudal Level (degrees) – Per Protocol Cohort

	prodisc L						Fusion						t-test	Wilcoxon	Effect
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p-value†	p-value‡	size§
Baseline	153	6.0	4.0	5.0	0.0	16.0	63	7.9	5.1	7.0	0.0	21.0	0.004	0.015	-0.41
Week 06	147	3.6	2.6	3.0	0.0	12.0	14	1.7	2.5	1.0	0.0	9.0	0.011	0.001	0.74
Month 03	145	4.2	2.9	4.0	0.0	12.0	26	1.1	0.8	1.0	0.0	4.0	<.001	<.001	1.46
Month 06	141	5.0	3.1	5.0	0.0	14.0	56	1.4	1.6	1.0	0.0	6.0	<.001	<.001	1.44
Month 12	132	5.4	3.8	5.0	0.0	18.0	58	1.1	1.2	1.0	0.0	5.0	<.001	<.001	1.53
Month 18	131	5.5	4.0	5.0	0.0	18.0	45	1.2	1.1	1.0	0.0	6.0	<.001	<.001	1.47
Month 24	139	6.0	4.2	5.0	0.0	23.0	60	1.0	1.3	1.0	0.0	6.0	<.001	<.001	1.61
Month 36	98	5.2	3.6	4.0	0.0	14.0	39	0.7	0.8	1.0	0.0	4.0	<.001	<.001	1.73
Month 48	83	5.0	3.4	4.0	0.0	15.0	27	0.5	0.6	0.0	0.0	2.0	<.001	<.001	1.85
Month 60	118	5.7	4.0	5.0	0.0	20.0	51	0.8	1.0	1.0	0.0	4.0	<.001	<.001	1.68

Notes:
† Two-sample pooled t-test p-value;
‡ Two-sample Wilcoxon rank sum p-value;
§ Standardized effect size (calculated as group difference in means divided by pooled within group SD).

At all timepoints after surgery, pro**disc**® L subjects had greater ROM than fusion subjects for both cranially and caudally implanted devices.

ROM was either stable or improved over time in the pro**disc**® L group compared to the Fusion group at both the cranial and caudal levels. These results reflect the fact that the pro**disc**® L devices allow some ROM. A decrease in rotation from baseline was seen at all time points for the control group at the level of the caudal implant, while there was an overall maintenance of motion in the pro**disc**® L group.

As assessment of change in ROM from baseline at the Month 24 and Month 60 time points is presented in Table 37.

Table 37: prodisc® L ROM Change from Baseline – Per Protocol Cohort

			Month 24[1]	Month 60[1]
Randomized prodisc® L (per protocol) N=161	Cranial (superior) Level	Increased (>3°)	43 (31.9%)	25 (21.9%)
		Maintained (≥-3° to ≤3°)	77 (57.0%)	70 (61.4%)
		Decreased (<-3°)	15 (11.1%)	19 (16.7%)
		Missing Δ[2]	26	47
	Caudal (inferior) Level	Increased (>3°)	30 (22.9%)	21 (18.9%)
		Maintained (≥-3° to ≤3°)	74 (56.5%)	60 (54.1%)
		Decreased (<-3°)	27 (20.6%)	30 (27.0%)
		Missing Δ[3]	30	50
	Combined	Increased (>3°)	51 (38.9%)	33 (29.7%)
		Maintained (≥-3° to ≤3°)	46 (35.1%)	46 (41.4%)
		Decreased (<-3°)	34 (26.0%)	32 (28.8%)
		Missing Δ[4]	30	50

[1]Percentages reported are of subjects with data. Month 24: n=135 cranial, n=131 caudal/combined. Month 60: n=114 cranial, n=111 caudal/combined.
[2]Includes n=5 subjects with missing baseline cranial ROM data.
[3]Includes n=8 subjects with missing baseline caudal ROM data.
[4]Includes n=8 subjects with missing baseline combined ROM data.

Overall, 88.9% of prodisc® L subjects with ROM data at 24 months experienced an increase or maintenance in ROM (defined as a decrease no more than 3° from pre-operative measurement) at the cranial level. In addition, 79.4% of prodisc® L subjects with ROM data at 24 months experienced an increase or maintenance in ROM at the caudal level. In combined ROM (summing the ROM from the 2 treated motion segments), 74.0% of prodisc® L subjects with ROM data at 24 months experienced an increase or maintenance in combined ROM.

Bridging Bone and Heterotopic Ossification

Bridging Bone of >50% is strong evidence of fusion. Fusion Status success in the prodisc® L group was defined as an absence of continuous connection of bridging bone between adjacent endplates. The qualitative scale used to evaluate bridging bone in prodisc® L subjects is summarized in Table 38.

Table 38: Bridging Bone and Heterotopic Ossification Qualitative Grading – prodisc® L Group

0 - None	No evidence of osteophyte formation or heterotopic ossification.
1 - Mild	Isolated points of initial hyperostosis or islands of bone in soft tissue.
2 - Moderate	Bony protrusions project more or less horizontally from the vertebral body. Bone does not occur within the disc space (planes formed by the two adjacent endplates).
3 - Severe	Bone occurs between the two planes formed by the vertebral endplates but does not bridge. Osteophytes assume the characteristic bird's beak shape, curving in the direction of the intervertebral disc and may come into contact with osteophytes on adjacent
4 - Bridging Bone *	An apparent continuous connection of bridging bone exists between the adjacent endplates. Osteophytes of adjacent vertebrae appear fused, thereby forming a bony bridge across the intervening joint.
5 - Indeterminate	Insufficient data to perform assessment

* Note: Grade '4' must be accompanied with quantitated motion at the implanted level of ≤2-degrees. Cases where motion is >2-degrees were determined to be grade '3'.

Mild to moderate (Class 1 and 2) Heterotopic Ossification (HO) following lumbar total disc arthroplasty procedures do not generally limit motion at the treated surgical level. In contrast, severe HO and bridging bone (Class 3 and 4) may restrict motion at the treated level.

Table 39: Heterotopic Ossification – Cranial Level, prodisc® L Group – Per Protocol Cohort

	Month 12		Month 24		Month 36		Month 48		Month 60	
	prodisc L		prodisc L		prodisc L		prodisc L		prodisc L	
	n	%	n	%	n	%	n	%	n	%
None	132	97.8%	126	89.4%	89	88.1%	69	81.2%	91	75.8%
Mild	1	0.7%	6	4.3%	6	5.9%	6	7.1%	9	7.5%
Moderate	0	0.0%	5	3.5%	2	2.0%	3	3.5%	10	8.3%
Severe	1	0.7%	4	2.8%	3	3.0%	6	7.1%	9	7.5%
Bridging Bone	0	0.0%	0	0.0%	1	1.0%	1	1.2%	1	0.8%
Indeterminate	1	0.7%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Not Assessed	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%

Table 40: Heterotopic Ossification – Caudal Level, prodisc® L Group – Per Protocol Cohort

	Month 12		Month 24		Month 36		Month 48		Month 60	
	prodisc L		prodisc L		prodisc L		prodisc L		prodisc L	
	n	%	n	%	n	%	n	%	n	%
None	135	100.0%	139	98.6%	101	100.0%	83	97.6%	115	95.8%
Mild	0	0.0%	1	0.7%	0	0.0%	1	1.2%	1	0.8%
Moderate	0	0.0%	1	0.7%	0	0.0%	1	1.2%	4	3.3%
Severe	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Bridging Bone	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Indeterminate	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Not Assessed	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%

No pro**disc**® L subjects exhibited evidence of bridging bone at Month 24. Throughout the course of the 5-year study, three pro**disc**® L subjects exhibited evidence of bridging bone, all of which occurred after Month 24 and in the cranially implanted device level (Table 39).

Table 41: Bridging Bone – Cranial Level, Fusion Group – Per Protocol Cohort

	Month 12		Month 24		Month 36		Month 48		Month 60	
	Fusion		Fusion		Fusion		Fusion		Fusion	
	n	%	n	%	n	%	n	%	n	%
None	16	26.7%	5	8.3%	4	10.3%	4	13.8%	4	7.8%
Bridging Bone	44	73.3%	55	91.7%	35	89.7%	25	86.2%	47	92.2%
Indeterminate	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Not Assessed	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%

Table 42: Bridging Bone – Caudal Level, Fusion Group – Per Protocol Cohort

	Month 12		Month 24		Month 36		Month 48		Month 60	
	Fusion		Fusion		Fusion		Fusion		Fusion	
	n	%	n	%	n	%	n	%	n	%
None	13	21.7%	10	16.7%	3	7.7%	0	0.0%	4	7.8%
Bridging Bone	47	78.3%	50	83.3%	36	92.3%	30	100.0%	47	92.2%
Indeterminate	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Not Assessed	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%

In the Fusion group, fusion status was assessed at Month 12 onwards as an apparent continuous connection of bridging bone between adjacent endplates. Evidence of bridging bone was assessed at every time point. There were some patients that exhibited bridging bone at either the cranial or caudal level, but not both. At Month 24, evidence of interbody fusion by bridging bone at both cranial and caudal levels was achieved in 81.7% (49/60) of Fusion subjects. At Month 60, bridging bone at both cranial and caudal levels was achieved in 88.2% (45/51) of Fusion subjects.

Disc Height

Disc height success was defined as no loss of disc height > 3mm. Disc height change over time for cranially implanted devices are outlined in Table 43. Disc height change over time for caudally implanted devices are outlined in Table 44.

Table 43: Descriptive Statistics for Disc Height – Cranial Level – Per Protocol Cohort

	prodisc L						Fusion						t-test	Wilcoxon	Effect
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p-value†	p-value‡	size§
Baseline	154	8.3	1.8	8.3	3.6	13.2	64	8.6	1.3	8.8	5.1	11.5	0.159	0.120	-0.22
Week 06	152	11.7	2.0	11.9	4.3	15.8	59	10.8	1.8	11.1	6.2	14.1	0.003	0.001	0.47
Month 03	149	11.7	1.9	11.7	3.7	15.4	63	10.6	1.8	10.9	5.9	14.1	<.001	<.001	0.55
Month 06	142	11.6	2.0	11.7	3.6	15.2	61	10.4	1.9	10.7	6.0	14.0	<.001	<.001	0.59
Month 12	134	11.4	2.1	11.5	3.5	15.4	60	10.4	2.1	10.6	5.7	14.1	0.001	<.001	0.51
Month 18	130	11.5	2.0	11.6	4.3	15.2	47	10.2	2.0	10.4	5.8	13.9	<.001	<.001	0.62
Month 24	140	11.5	2.0	11.6	4.3	15.7	60	10.2	2.0	10.4	5.8	14.0	<.001	<.001	0.63
Month 36	100	11.6	1.7	11.7	5.6	15.6	39	10.3	2.1	10.6	5.4	13.8	<.001	<.001	0.70
Month 48	85	11.6	1.9	11.5	5.4	15.5	30	9.9	2.0	9.8	5.5	13.3	<.001	<.001	0.84
Month 60	119	11.4	1.9	11.5	4.1	15.8	51	10.1	2.0	10.1	5.1	13.7	<.001	<.001	0.66

Notes:
† Two-sample pooled t-test p-value;
‡ Two-sample Wilcoxon rank sum p-value;
§ Standardized effect size (calculated as group difference in means divided by pooled within group SD).

Table 44: Descriptive Statistics for Disc Height – Caudal Level – Per Protocol Cohort

	prodisc L						Fusion						t-test	Wilcoxon	Effect
	N	Mean	SD	Med	Min	Max	N	Mean	SD	Med	Min	Max	p-value†	p-value‡	size§
Baseline	154	7.5	2.0	7.4	3.5	13.5	63	7.9	1.9	7.9	3.7	11.9	0.286	0.179	-0.16
Week 06	152	13.0	1.6	12.9	8.4	18.0	59	10.6	2.1	10.8	5.8	15.2	<.001	<.001	1.31
Month 03	149	12.9	1.5	12.9	8.7	18.0	63	10.5	2.0	10.6	6.1	15.3	<.001	<.001	1.34
Month 06	142	12.9	1.5	12.8	8.7	18.2	61	10.2	2.1	10.1	5.8	15.3	<.001	<.001	1.46
Month 12	134	13.0	1.5	12.9	8.6	18.7	60	10.1	2.3	10.1	5.3	15.3	<.001	<.001	1.45
Month 18	130	13.0	1.6	12.9	9.0	18.7	47	9.8	2.1	9.6	5.1	14.3	<.001	<.001	1.71
Month 24	140	12.9	1.6	12.8	8.7	19.0	60	10.0	2.3	9.9	5.6	15.7	<.001	<.001	1.45
Month 36	100	12.7	1.6	12.5	8.7	19.2	39	9.7	2.3	9.4	5.9	14.8	<.001	<.001	1.46
Month 48	85	12.7	1.6	12.6	8.8	18.8	30	9.9	2.6	10.0	5.7	15.8	<.001	<.001	1.30
Month 60	119	12.7	1.5	12.7	8.6	18.9	51	10.1	2.4	10.1	5.7	15.7	<.001	<.001	1.34

Notes:
† Two-sample pooled t-test p-value;
‡ Two-sample Wilcoxon rank sum p-value;
§ Standardized effect size (calculated as group difference in means divided by pooled within group SD).

Post-surgery, although there was a statistically significant difference between the mean disc height of the groups, this difference was attributed to the differences in implant size. Between Week 6 and Month 60, there was a 0.3 mm loss of mean disc height for the pro**disc**® L group and 0.5 mm loss for the fusion group. This difference was not considered to be clinically meaningful and below the ±3 mm margin of error of the plain radiographs analyzed.

Migration

Migration was defined as device translation >3mm in the anterior or posterior direction, parallel to the affected endplate.

Throughout the course of the 5-year study, one pro**disc**® L subject was a failure due to device migration, which was noted during independent radiographic review of films from the 6-week visit. The subject was subsequently revised to fusion.

No Fusion subjects were considered migration failures during the 5-year study.

Radiolucency

Radiolucency success was defined as no radiolucency >25% of the length of the implant/bone interface. The qualitative scale used to evaluate radiolucency is summarized in Table 45.

Table 45: Radiolucency Qualitative Grading

0 - None	Absence of radiolucent lines or halos along the bone-implant interface
1 - Mild	<25% radiolucent lines along the bone-implant interface
2 - Moderate	25-49% radiolucent lines along the bone-implant interface
3 - Severe	≥ 50% radiolucent lines along the bone-implant interface
4 - Indeterminate	Insufficient information to complete this assessment

Radiolucency events involving the cranially implanted device levels are outlined in Table 46, while events involving the caudally implanted device levels are outlined in Table 47.

Table 46: Radiolucency – Cranial Level – Per Protocol Cohort

	Week 06				Month 03				Month 06				Month 12			
	prodisc L		Fusion		prodisc L		Fusion		prodisc L		Fusion		prodisc L		Fusion	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
None	154	100.0%	60	98.4%	150	99.3%	64	98.5%	141	99.3%	61	100.0%	134	99.3%	60	100.0%
Mild	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Moderate	0	0.0%	1	1.6%	0	0.0%	1	1.5%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Severe	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Indeterminate	0	0.0%	0	0.0%	1	0.7%	0	0.0%	1	0.7%	0	0.0%	1	0.7%	0	0.0%
Not Assessed	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
	Month 24				Month 36				Month 48				Month 60			
	prodisc L		Fusion		prodisc L		Fusion		prodisc L		Fusion		prodisc L		Fusion	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
None	141	100.0%	60	100.0%	101	100.0%	39	100.0%	85	100.0%	29	100.0%	120	100.0%	49	96.1%
Mild	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	2.0%
Moderate	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Severe	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Indeterminate	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	2.0%
Not Assessed	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%

There were no occurrences of radiolucencies for cranially implanted pro**disc**® L devices (Table 46).

Table 47: Radiolucency – Caudal Level – Per Protocol Cohort

	Week 06				Month 03				Month 06				Month 12			
	prodisc L		Fusion		prodisc L		Fusion		prodisc L		Fusion		prodisc L		Fusion	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
None	154	100.0%	61	100.0%	151	100.0%	65	100.0%	142	100.0%	61	100.0%	135	100.0%	60	100.0%
Mild	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Moderate	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Severe	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Indeterminate	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Not Assessed	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
	Month 24				Month 36				Month 48				Month 60			
	prodisc L		Fusion		prodisc L		Fusion		prodisc L		Fusion		prodisc L		Fusion	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
None	141	100.0%	60	100.0%	101	100.0%	39	100.0%	84	98.8%	30	100.0%	119	99.2%	51	100.0%
Mild	0	0.0%	0	0.0%	0	0.0%	0	0.0%	1	1.2%	0	0.0%	1	0.8%	0	0.0%
Moderate	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Severe	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Indeterminate	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Not Assessed	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%

Over five years of follow-up, mild cases of radiolucencies in the caudally implanted were noted in one pro**disc**® L subject at both the Month 48 and Month 60 time points (Table 47).

Subsidence

An analysis of subsidence was conducted using a definition of adverse motion of the device >3 mm in the cranial (in the superior direction) or caudal (in the inferior direction) direction, perpendicular to the affected endplate. Subsidence events occurring at the cranially implanted device levels are summarized in Table 48, while events occurring at the caudally implanted device levels are outlined in Table 49.

Table 48: Subsidence – Cranial Level – Per Protocol Cohort

	Week 06				Month 03				Month 06			
	prodisc L		Fusion		prodisc L		Fusion		prodisc L		Fusion	
	n	%	n	%	n	%	n	%	n	%	n	%
None (<3mm)	150	97.4%	61	100.0%	146	96.7%	65	100.0%	136	95.8%	61	100.0%
Yes; Cranial	2	1.3%	0	0.0%	2	1.3%	0	0.0%	2	1.4%	0	0.0%
Yes; Caudal	2	1.3%	0	0.0%	2	1.3%	0	0.0%	3	2.1%	0	0.0%
Indeterminate	0	0.0%	0	0.0%	1	0.7%	0	0.0%	1	0.7%	0	0.0%
Not Assessed	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%

	Month 12				Month 24				Month 36			
	prodisc L		Fusion		prodisc L		Fusion		prodisc L		Fusion	
	n	%	n	%	n	%	n	%	n	%	n	%
None (<3mm)	129	95.6%	59	98.3%	136	96.5%	59	98.3%	99	98.0%	38	97.4%
Yes; Cranial	2	1.5%	1	1.7%	2	1.4%	1	1.7%	2	2.0%	1	2.6%
Yes; Caudal	3	2.2%	0	0.0%	3	2.1%	0	0.0%	0	0.0%	0	0.0%
Indeterminate	1	0.7%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Not Assessed	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%

Month 48				Month 60			
prodisc L		Fusion		prodisc L		Fusion	
n	%	n	%	n	%	n	%
83	97.6%	28	96.6%	117	97.5%	51	100.0%
2	2.4%	1	3.4%	2	1.7%	0	0.0%
0	0.0%	0	0.0%	1	0.8%	0	0.0%
0	0.0%	0	0.0%	0	0.0%	0	0.0%
0	0.0%	0	0.0%	0	0.0%	0	0.0%

Over five years of follow-up, there was a low rate of subsidence in the cranial (superior) implant with a 3.5% rate at month 24 and 2.5% rate at month 60. There were no reports of re-operation in any of these cases.

Table 49: Subsidence – Caudal Level – Per Protocol Cohort

	Week 06				Month 03				Month 06			
	prodisc L		Fusion		prodisc L		Fusion		prodisc L		Fusion	
	n	%	n	%	n	%	n	%	n	%	n	%
None (<3mm)	152	98.7%	61	100.0%	149	98.7%	65	100.0%	141	99.3%	61	100.0%
Yes; Cranial	2	1.3%	0	0.0%	2	1.3%	0	0.0%	1	0.7%	0	0.0%
Yes; Caudal	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Indeterminate	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Not Assessed	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%

Month 12				Month 24				Month 36			
prodisc L		Fusion		prodisc L		Fusion		prodisc L		Fusion	
n	%	n	%	n	%	n	%	n	%	n	%
134	99.3%	60	100.0%	140	99.3%	60	100.0%	101	100.0%	39	100.0%
1	0.7%	0	0.0%	1	0.7%	0	0.0%	0	0.0%	0	0.0%
0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%
0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%	0	0.0%

Month 48				Month 60			
prodisc L		Fusion		prodisc L		Fusion	
n	%	n	%	n	%	n	%
85	100.0%	30	100.0%	120	100.0%	51	100.0%
0	0.0%	0	0.0%	0	0.0%	0	0.0%
0	0.0%	0	0.0%	0	0.0%	0	0.0%
0	0.0%	0	0.0%	0	0.0%	0	0.0%
0	0.0%	0	0.0%	0	0.0%	0	0.0%

Over five years of follow-up, there was a low rate of subsidence in the caudal (inferior) implant with a rate of 0.7% at Month 24. There were no reports of re-operation in these subjects. All of the occurrences of subsidence were in the cranial direction.

E. Financial Disclosures

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 49 investigators of which none were full-time or part-time employees of the sponsor and 19 had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 2 investigators
- Significant payment of other sorts: 12 investigators
- Proprietary interest in the product tested held by the investigator: 0 investigators
- Significant equity interest held by investigator in sponsor of covered study: 14 investigators

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XI. PANEL RECOMMENDATIONS

In accordance with the provisions of section 515(c)(2) of the Act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Orthopaedic and Rehabilitation Devices Panel, an FDA advisory committee, for review and recommendation.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

The valid scientific evidence presented in the preceding sections provides reasonable assurance that the pro**disc**® L is a safe and effective disc replacement for spinal arthroplasty in skeletally mature patients with degenerative disc disease (DDD) at one or two contiguous intervertebral level(s) from L3-S1. DDD is defined as discogenic back pain with degeneration of the disc confirmed by patient history and radiographic studies. These DDD patients should have no more than Grade 1 spondylolisthesis at the involved level(s). Patients receiving the pro**disc**® L Total

Disc Replacement should have failed at least six months of conservative treatment prior to implantation of the pro**disc**® L Total Disc Replacement.

A. Effectiveness Conclusions

Two hundred fifty-five (255) subjects were randomized under the pro**disc**® L IDE study, with 164 subjects randomized to pro**disc**® L and 72 subjects randomized to Fusion. Nineteen (19) subjects (9 randomized to pro**disc**® L and 10 randomized to Fusion) were withdrawn prior to surgery resulting in 236 subjects treated, comprising 164 pro**disc**® L and 72 Fusion subjects. Seven (7) subjects (3 pro**disc**® L and 4 Fusion) were deemed major protocol violators. The remaining per protocol population resulted in 229 subjects (161 pro**disc**® L and 68 Fusion). Analysis of subject demographic and baseline data showed no meaningful differences between the treatment groups. Mean surgery time was on average 114 minutes longer for the control Fusion group than for the pro**disc**® L group, and mean hospital stay was 1.2 days longer for the control Fusion group than for the pro**disc**® L group.

Overall success was defined based on the FDA-requested primary endpoints, which included the following components: lack of secondary surgical interventions (SSI), lack of new neurological deficit, a clinically meaningful improvement in ODI (i.e. at least 15 points), improvement in SF-36, and radiographic success (both with and without a ROM component).

- Using the FDA-requested primary endpoint, overall success at 24 months for pro**disc**® L (with the ROM component) was 55.9% compared to 46.7% for Fusion.

- After removing the ROM component of the primary endpoint, FDA-requested overall success at 24 months for pro**disc**® L was 62.9% compared to 46.7% for Fusion.

- Non-inferiority was statistically demonstrated from these data. Primary endpoint data collected through 60 months supports these results.

To assess the impact of subjects with unknown outcomes or other potential biases, various sensitivity analyses were conducted. While these analyses were conducted, they did not impact the overall outcome of non-inferiority.

In conclusion, the study data indicate that, through 60 months post-operatively, the pro**disc**® L is at least as effective as the control treatment (Fusion), for the patient population and indications studied in this investigation, in terms of overall success according to the FDA-specified primary endpoint.

B. Safety Conclusions

The risks of the device were based on nonclinical bench testing as well as data collected in a clinical study (G010133) conducted to support PMA approval as described above. The safety analysis included five-year data from a well-controlled, pivotal clinical trial.

Preclinical testing performed on the device demonstrated that the pro**disc**® L is designed to withstand the expected physiologic loads in the lumbar spine.

In the clinical study conducted to support this PMA approval, the pro**disc**® L was found to have a reasonable assurance of safety and to be at least as safe as the control treatment. This safety assessment considers Adverse Event rates (AEs), Subsequent Surgical Interventions (SSI), and Neurological Success.

Specifically, the observed AE rate for the pro**disc**® L group was 92.7% (153/165) compared with 97.2% (70/72) in the Fusion group. The rate of severe or life-threatening AEs was 24.8% (41/165) in the pro**disc**® L group and 36.1% (43/72) in the Fusion group.

The observed device or surgery-related AE rate for the pro**disc**® L group was 60.0% (99/165) compared to 68.1% (49/72) in the Fusion group. The rate of severe or life-threatening device or surgery-related AEs was 7.9% (13/165) in the pro**disc**® L group and 22.2% (16/72) in the Fusion group.

The SSI rate for the pro**disc**® L group through the 60-month follow-up was lower than the Fusion control group. Specifically, 3.1% (5/161) pro**disc**® L subjects required SSIs at the treated level compared to 17.6% (12/68) of the Fusion control subjects.

The neurological success rate for the pro**disc**® L group was 88.0% (110/125) and 81.1% (43/53) for the Fusion control group at the 60-month follow-up time point.

In conclusion, the safety profile of the pro**disc**® L implanted in the lumbar spine for treatment of two-level DDD demonstrates that the device has a reasonable assurance of safety and is at least as safe as the control Fusion treatment in regards to adverse event rates, neurologic status, and the need for subsequent surgical intervention.

C. Benefit-Risk Conclusions

The probable benefits of the pro**disc**® L for implantation at two contiguous vertebral levels are based on data collected in the clinical study conducted to support PMA approval. The clinical study demonstrated several benefits of the pro**disc**® L performed at two lumbar vertebral levels over 24 months and these benefits continued through 60 months based on additional data collected.

- The benefit of the pro**disc**® L in terms of clinically meaningful improvement in function (as measured by an improvement in ODI of at least 15 points) at 24 months post-operatively, pro**disc**® L subjects demonstrated a higher rate of improvement when compared to the standard of care, Fusion, (72.7% of pro**disc**® L subjects and 57.4% of Fusion subjects). At 60 months post-operatively, a similar higher rate of improvement was shown (70.6% of pro**disc**® L subjects and 60.4% of Fusion subjects).

- In terms of improvement in back pain (as measured by a 20 mm improvement in pain on a Visual Analog Scale as compared to baseline), at 24 months post-operatively, pro**disc**® L subjects demonstrated a statistically significant difference relative to the standard of

care, Fusion, (73.9% of pro**disc**® L subjects and 60.7% of Fusion subjects with low back and leg pain improvement at 24 months).

- The subject's perception of their benefit and risk was indirectly measured using a Visual Analog Scale and by asking the subjects if whether they would have the surgery again. At 24 months following the index procedure, the mean subject satisfaction as measured by VAS was 78.3 in the pro**disc**® L group and 66.2 in the Fusion group, while 79.1% of pro**disc**® L subjects answered they would have the surgery again compared to 66.1% of Fusion subjects.

- In the pro**disc**® L group, ROM was maintained over the follow-up period, with 74.0% of pro**disc**® L subjects with ROM data at 24 months experienced an increase or maintenance in combined ROM, and 71.2% at 60 months. Comparatively, the ROM in the Fusion group decreased. This is expected when comparing a motion-preserving device (artificial lumbar disc) versus a motion-eliminating device (Fusion).

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval. The risks of pro**disc**® L when used at two spinal levels are similar to those of when pro**disc**® L is used at one level, which include systemic, surgery-related and device-related adverse events and subsequent surgical interventions. Through the 60-month time-point, higher rates of any adverse event, any severe or life-threatening adverse event, and surgery related adverse events occurred in the Fusion group. At the same time-point, there were similar rates of device-related adverse events in the pro**disc**® L and Fusion groups. In addition, there were fewer subsequent surgical interventions at the index levels in the pro**disc**® L group compared to the Fusion control group. With respect to subsequent surgical interventions, only 4/161 (2.5%) pro**disc**® L subjects and 7/68 (10.3%) control subjects reported subsequent surgical interventions qualifying as study failures (i.e., at the index levels) through 24 months, and 3.1% (5/161) pro**disc**® L subjects reported subsequent surgical interventions at the treated level compared to 17.6% (12/68) control subjects through 60 months.

Additional factors considered in determining benefits and risks for the pro**disc**® L at two consecutive lumbar levels included: limitations of the clinical study design, including the inability to mask subjects to their treatment assignment, reliance on subjective endpoints, and subjectivity in adverse event classification.

In addition, sensitivity analyses were performed to address the missing data as well as the generalizability of the study results. These sensitivity analyses support the robustness of the non-inferiority result with respect to missing data and demonstrate that the results are generalizable to the overall population studied.

Specific information on subject perspectives for this device was not directly measured. However, the subjects' perception of their benefit and risk was indirectly measured through a questionnaire asking if they would have the surgery again, as described above.

In conclusion, given the available information above, the data support that for the pro**disc**® L at two consecutive lumbar levels (L3-S1), the probable benefits outweigh the probable risks.

D. Overall Conclusions

The non-clinical and clinical data in this application support the reasonable assurance of safety and effectiveness of pro**disc**® L when used in accordance with the indications for use. Based on the clinical study results, it is reasonable to conclude that the clinical benefits of the use of pro**disc**® L in terms of improvement in pain and disability, and the potential for motion preservation, outweigh the risks, both in terms of the risks associated with pro**disc**® L and surgical procedure when used in the indicated population in accordance with the directions for use, and as compared to the Fusion control treatment in the same indicated population.

XIII. CDRH DECISION

CDRH issued an approval order on April 10, 2020.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for Use: See device labeling

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See Approval Order.